Original Articles.

THE ACTION OF LECITHIN UPON TUBERCLE BACILLI AND THEIR RELATION TO EXPERIMENTAL TUBERCULOSIS.*

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AND

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KOCH's discovery of tuberculin opened a new field for a specific treatment of tuberculosis, although the expectations that were aroused were not fulfilled completely. After a time of skepticism and discouragement, many investigators pursued the line of thought expressed by their master, so leading up to new ideas and a better understanding of the aims of a specific treatment. In the course of the passing years we have learned about the complex nature of the tubercle bacillus. As seen from the work of Deycke and Much (*Muench. med. Wochenschr.*, 1909, No. 39; *Med. Klinik*, 1908, No. 40); Much, (*Muench med. Wochenschr.*, 1912, p. 685) the tubercle bacillus is thought to consist of four different substances, namely proteids, fatty acids and lipoids, neutral fat and the toxin itself, which substances have all an important influence in the course of the tubercular infection. Various authors in following Much's indications have succeeded in the attenuation of virulent tubercle bacilli by treating these organisms with lecithin (Much, *loc. citat.*), cholin, neurin (G. Deycke, *Muench. med. Wochenschr.*, 1910, p. 633, No. 12; Much, *ibid.*, 1910, p. 1093, No. 20; Ditthorn, *Berl. klin. Wochenschr.*, No. 34, 1910; Lindemann, *Ztschr. f. Immun. Forsch. u. Experiment. Therap.*, Vol vii; Leschke, *Beitr. z. Klin. d. Tuberculose*, Vol. xx, H. 3, 1912; K. Meyer, *Ztschr. f. Immun. Forsch. u. Experiment. Therap.*, Vol. xv, H. 2-3; *Muench. med. Wochenschr.*, 1912, p. 379). According to these investigators even a complete bacteriolysis was obtained. Compounds of cholin, borcholin (enzytol) had a similar effect (H. Mehler and Ascher, *Muench. med. Wochenschr.*, 1913, p. 748, No. 14). Trichlorethylene besides neurin, as well as other strong basic ammonia compounds (Aronson, Berl. Medic. Soc., July 7-13, 1910, ref. *Muench. med. Wochenschr.*, 1910) also caused a bacteriolysis, as well as organic and inorganic acids (Much, *Muench, med. Wochenschr*, 1911, p. 597; E. Leschke, *ibid.*, p. 598; *Beitr. Klin.* d. *Tuberculose*, Vol. xx, H. 3, 1912). The latter substances were found more suitable for the immunizing action of the split products obtained.

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In a previous study upon the influence of fresh and autolyzed organ extracts on experimental tuberculosis (Charles William White and E. Zueblin, *Jour. Infect. Dis.*, Vol. viii, No. 2, March, 1911) we reached the conclusion that bovine tubercle bacilli underwent an attenuation when treated with autolyzed organ extracts. This action was especially noticeable with lung extract, less for liver extract. It was also possible to demonstrate in the autolyzed fluid the presence of cholin (a split product of lecithin). At the same time tubercle bacilli left in extract with the autolyzed fluid lost their acid fastness and became granular.

The present report is a continuation of our study and deals with the morphological and biologic changes of the tubercular virus when treated with lecithin. Our study can be divided into categories:—

(*a*) The staining properties of human, bovine and avian tubercle bacilli treated with mixtures of lecithin.

(*b*) The biological qualities of human and bovine tubercle bacilli after treatment with lecithin.

Staining properties of human, bovine and avian tubercle bacilli treated with mixtures of lecithin. In the report the following technic was resorted to.

1.5 gr. tubercle bacilli were mixed together in a sterile mortar with 2 ampules of lecithin (Billon). The mixture was subdivided in 3 equal parts into sterile ampules. These ampules were kept for one-half hour at 70 respt. at 50° in the water bath. After that time they were incubated with the 3d unheated portion at 37° and left in the thermostat for three successive days. After the lapse of that time one 0.7 c.c. of each ampule was injected intraperitoneally as recorded in the second part of our experiment. Before this was done, untreated tubercle bacilli were stained according to the usual laboratory method and compared with smears made from the contents of the ampules. The staining method consisted briefly in the following:

1 c.c. carbol gentian violet with 4 c.c. of carbol fuchsin were mixed, and with that stain the preparation on the slide was steamed for two minutes. The excess of stain was then thrown off, the slide immersed into Lugol's solution, left in contact a few minutes, then the slide was decolorized with a mixture consisting of alcohol 50%, aceton 50%, nitric acid 3%. After the decolorizing had been carried out to the point that all excess stain was removed, the slide was washed in running water and counterstained with methylin blue.

The slides were also stained according to Ziehl's method with the same result. It seemed, however, that with the above-mentioned carbol gentian violet and fuchsin stain the morphological and tinctorial changes were more distinct.

Normal, untreated human tubercle bacilli treated in that way showed the characteristic fast properties of the bacillus without the presence of any degenerate forms as the granules indicated by Much.

In the preparation, however, made from the lecithin mixtures such degenerate forms were noticed, particularly in the human tubercle bacilli, so f.i. H 37 on several slides presented a few normal stained red bacilli. Most of the remaining organisms, however, presented a loss in the acid-fast quality. In some instances only unstained protoplasm remained, which surrounded the thick granules occupying the centre of the organisms. At a later stage the pink color had changed into purple, and even a few purple granules were the only remnants of the tubercle bacilli. Such a character was found more pronounced in the slides prepared from H 50. These changes were more pronounced a few days later from the smears prepared from the mixtures incubated.

Bovine tubercle bacilli treated in the above indicated manner presented at a temperature of 37° not such pronounced changes. The majority of the organisms maintained their acid-fast character; only a few granular or purple stained forms could be noticed. That change was more pronounced on the slides prepared from B. 50, but compared with the human strain treated similarly the changes were never so pronounced. Avian tubercle bacilli were treated in a similar manner and they also presented the granular aspect.

From a comparison of the human tubercle bacilli with the bovine strain it would seem that the human form is more readily affected by the lecithin. This effect is more marked if the mixtures are kept at a higher temperature, and the longer they remain in contact with the lipoid substance. A portion of the lecithin human tubercle bacillary emulsion was treated with 5% antiformin solution, then washed with ether. The solution containing the fatty substances retained an acid-fast stain, whilst the bacilli did not retain the carbol fuchsin.

It seemed of interest to inoculate these lecithin mixtures into guinea-pigs, which reacted as follows:—

B. BIOLOGICAL QUALITIES OF HUMAN AND BOVINE TUBERCLE BACILLI AFTER-TREATMENT WITH LECITHIN.

CONTROLS FOR BOTH SERIES—(A AND B).

Guinea-pig No. 13, control. Infected with 0.1 gm. human tubercle bacilli, weighed 320 gm. lived 50 days and lost 40 gm.

Post-mortem showed: Peritoneum thickened, of granular aspect, injected parietal peritoneum presents several tubercles in tubes and ligamentum, mensentery gland enlarged, several miliary and conglomerate tubercles in liver, spleen considerably enlarged with many tubercles; diaphragm, interior surface many big tubercles; lungs, several tubercles scattered over all lobes; pleura clean, bronchial glands enlarged.

Guinea-pig No. 14, control. Weighed 550 gm. when injected with .01 gm. human tubercle bacilli. It lived 31 days and lost 125 gm.

Animal was much emaciated and presented at the post-mortem a caseous mass (abscess formation in the abdominal wall of hickory nut size), surface of peritoneum uneven, granular with scattered fine tubercles. Mesentery glands, inguinal glands enlarged, no fluid in the abdominal cavity, intestines, diaphragm free from tubercles, liver hyperemic with 5 caseous tubercles, spleen granular border, a few small tubercle nodules, kidneys hyperemic, glistening surface, no tubercles; lung, both upper lobes present numerous single and conglomerate tubercles; a few tubercles in the right middle lobe, single and conglomerate tubercles along the upper border of the lower lobes; pleura free from tubercles; bronchial glands enlarged, thymus enlarged, presents a few white tubercles.

(A) HUMAN TUBERCLE BACILLI.

1. *Human Tubercle Bacilli* 70° + *Lecithin.*

Guinea-pig No. 1. Before first reinfection gained after 3 weeks 115 gm., then showed slight loss in weight, 45 gm. during the first week, which loss was overcome in the following weeks. After the second reinfection an increase in weight until 2 weeks prior to exitus was noted, then a rapid loss of 250 gm. took place. The animal outlived the two control animals 110 days, and after infection remained alive 258 days.

Post-mortem: Lymph glands not enlarged, with the exception of the mesentery glands which were increased in size. Diaphragm, heart, pleura, peritoneum free from tubercular involvement. Liver enlarged, shows several yellowish and anemic patches. Tubercle infection at the border of the right lung; spleen large, hyperemic. Lungs, left lobe hyperemic, slight emphysema. Numerous patches in the right middle and upper lobe. Uterus enlarged, hyperemic, dry white fleshy lobule (2-mm.); dry, small lobule on the right corn, remaining adnexa free from tubercle involvement. The animal seemed very well, only a few weeks prior to its exitus a general decline could be noticed.

Guinea-pig No. 2. Lived 214 days, was reinfected twice, little affected by the first treatment, increased in weight 180 gm. after the first reinfection lost 60 gm., after the second reinfection became pregnant, which condition reached its normal time, but immediately afterwards a rapid decline could be noticed, and after reinfection died in 71 days. It outlived the control animal 40 days, but did not show any tubercle lesions.

The post-mortem showed the abdominal wall smooth, slightly injected peritoneum, broad ligaments and spleen, diaphragm, heart, lungs, kidneys and liver absolutely free from tubercle infection.

2. *Human Tubercle Bacilli* 50° + *Lecithin.*

Guinea-pig No. 3. Weight 490 gm., when injected with the emulsion, it lived 135 days. It was reinfected twice with .01 gm. human untreated tubercle bacilli on the 4th of March and on the 12th of June respt. It lost 40 gm. during the first two weeks following the first treatment, then gained in weight 20 gm.; after the first infection a slight decline in weight (15 gm.) was observed in 2 days. After the second reinfection the animal died (shock or pneumonia?). The tubercle lesions were less pronounced than in the control animal.

Post-mortem findings: Abdominal cavity contains a few c.c. of a cloudy hemorrhagic fluid and

a few yellow lumps; a fibrinous deposit over the large intestine and the great omentum were observed. Spleen and liver normal, lungs, a few spots of pneumonia in the middle and lower lobes and a few whitish yellow spots on both sides of the diaphragm; a few tubercles are found in both testicles (these organs were already enlarged several weeks preceding death. The tunica vaginalis propria shows several tubercles.

Guinea-pig No. 4. Weight when treated with the bacilli emulsion 500 gm. The animal was little affected by the first treatment, gained in weight 65 gm. After first reinfection loss in weight of 60 gm. during the first 3 weeks; on the following 55 days gained in weight, then declined until time of second reinfection, when a deficit in weight of 55 gm. was noticed. After the second reinfection up to his death lost ground, declined in weight (115 gm.) and died 67 days later. It remained alive 200 days after the first treatment, but 37 days after the control animal and the second reinfection. The anatomical lesions were not very much different from those observed in the control animal.

Post mortem: Animal much emaciated, vessels of the abdominal wall injected, miliary tubercles scattered over the abdominal peritoneum, over ligamentum latum, conglomerate large tubercle noticed; peritoneal fluid clouded, hemorrhagic, a few nodules in mesentery, mesentery glands enlarged, left kidney small with smooth surface, one tubercle in the medullary substance. Right kidney of larger size, pale in aspect, two tubercles in medullary, one tubercle in cortical substance. Spleen enlarged, contains many white spots and tubercular infarction at the border. Liver, several gelatinous patches on the surface, no distinct tubercles found. The diaphragm shows a few granular spots on the abdominal surface; a few scattered tubercles on the pleural aspect; a few white nodules on the pericardium, no changes in the myocardium. Lungs show big conglomerate tubercle, a few tubercles scattered over the lower lobes and particularly along the medial border; a few tubercles in the upper lobes. The bronchial glands are enlarged; the costal pleura seems free from tubercles.

3. *Human Tubercle Bacilli 37° + Lecithin.*

Guinea-pig No. 5. Initial weight 695 gm., when first treated, lived 288 days; loss in weight before reinfection was hardly noticeable; during the first reinfection the difference was 16 gm., after the second reinfection a slight gain took place, then a slow decline of 110 gm. It outlived the first reinfection 158 days, and it outlived the second control 128 days.

At the post-mortem the peritoneum shows injection but no tubercles; no tubercles in the intestines; the testicles are enlarged and present a few caseous tubercles, mesentery glands enlarged, mesentery itself free from tuberculosis. Liver enlarged, shows miliary tubercles of pinhead size, surface of the organ is irregular. Spleen enlarged with tuberculous infarction; kidneys, parenchymatous nephritis; diaphragm, abdominal aspect several white nodules in left pleural cavity, thickened irregular granular surface with adhesions with left lower lobe of the lung, particularly posteriorly where a big conglomerated caseous tubercle is found (cherry-size); several tubercles in the other lobes are present besides hyperemia; the right lung shows less involvement and few tubercles.

Guinea-pig No. 6. Initial weight 565 gm., lived in all 197 days; was infected once and showed: Gain in weight after the first treatment without any apparent symptom of disease at the moment of the first injection. It showed only a slight difference with the initial weight, after the only reinjection a slight increase in weight, and though apparently in good health, 61 days later suddenly declined, lost 345 gm. and died 63 days after the reinjection, or 33 days after the second control animal.

Post mortem: Showed few changes, namely—only enlargement of the inguinal glands, no fluid in the abdominal cavity and no signs of tuberculosis.

If any conclusions from the preceding experiments with human tubercle bacilli after treatment with lecithin are permitted it would seem that the organisms undergo some loss in virulence. Guinea pigs after treatment with these emulsions may be reinfected once or twice with .01 gm. untreated human tubercle bacilli; they outlive the control animal several months. These animals gain in weight and no clinical symptoms of tubercular involvement or a few pathological changes of chronic tuberculous results may be found at post mortem. The attenuation of the tubercle virus seems more complete if the lecithin and tubercle mixtures are kept at a higher temperature of 70°. The immunity against tuberculosis so acquired may be influenced by different extrinsic factors.

Overtaxing of the animals and loss of their reserve strength, repeated pregnancy at short intervals, may lower the resistance against a tubercular infection to such an extent that the animal dies from exhaustion. As seen later on, the bovine tubercle bacillus is more resistant towards lipoid bodies than the human strain.

(B) EXPERIMENTS WITH BOVINE TUBERCLE BACILLI + LECITHIN.

1. *Bovine 70° + Lecithin.*

Guinea-pig No. 7. Initial weight 630 gm., lived 56 days, during the first treatment the animal gained 16 gm. in weight. Infected 47 days after the first injection with .01 gm. bovine tubercle bacilli, a steady decline in weight took place, the animal lost in all 80 gm. when it died, 9 days after reinfection.

The post-mortem showed: Peritoneal wall injected, of granular surface with many tubercles, few cbm. of a cloudy fluid noticed, over left hypochondrium an adherent mass is found measuring 3 cm. x 1.5 x 0.5 cm. of yellowish aspect with peripheric injection of the capillaries. The large intestine is adherent with that mass. Another tumor is found in the hypochondrium measuring 8 x .5 cm. composed of granular tissue adherent with large omentum. The mesentery shows many tubercles. Liver presents several pin-head size tubercles and a few fibrinous threads. Spleen not enlarged but presents a few white spots. The diaphragm of granular aspect, a few white elevations noticed. Pleura, fluid in both sacks, in the lungs a few gelatine spots and few gray elevated yellowish tubercles scattered over the surface.

Guinea-pig No. 8. Initial weight 540 gm., outlived first treatment 77 days; it was reinfected only

once at the same time as No. 7. During the first period, before reinfection, a gradual increase in weight of 80 gm. was noticed; after reinfection with .01 gm. bovine tubercle bacilli the animal declined rapidly and died 30 days after the reinfection, total difference in weight from beginning 10 gm. Unfortunately no post-mortem of that animal could be made.

2. *Bovine Tubercle Bacilli* 50° + *Lecithin.*

Guinea-pig No. 9. Lived 72 days after first treatment, was reinfected once, initial weight 620 gm.; after the first treatment the animal lost in weight 60 gm.; when it was reinfected, 33 days later, with .01 gm. bovine tubercle bacilli a slight increase in weight took place during the following first two weeks, then the animal declined rapidly, and at his death, 72 days after the first, 39 days after the second infection, the total loss was 190 gm.

Post-mortem: Animal much emaciated, in peritoneal cavity fluid present, peritoneal surface glistening, omentum thickened with a few granular nodules, inguinal and mesentery glands enlarged with a few yellowish white nodules, general hyperemia of the organ; liver of granular surface (cirrhotic) with many yellow fatty spots and tubercles. Diaphragm, several tubercles on both aspects. Lungs, many tubercles in left lobe, in the middle and lower right lobe with more pronounced involvement along the medial aspect; the right lobe shows less involvement, the trachial glands are enlarged, a few yellowish spots are noticed in the mesentery; kidneys congested but no macroscopic tuberculosis found.

Guinea-pig No. 10. Was treated in the same way as the previous number, reinfected 33 days after the first injection with .01 gm. bovine tubercle bacilli. During the first period the animal, after at first considerable loss in weight (50 gm.), remained at the same weight. After reinfection the animal increased again, and 84 days after beginning of the experiment that animal presented its initial weight. Owing to unfortunate circumstances further observations of the animal were impossible.

3. *Bovine Tubercle Bacilli* 37° + *Lecithin.*

Guinea-pig No. 11. Weighed 865 gm. when it was injected with the emulsion. It lived 151 days in all. It became pregnant two weeks after reinfection and gained in weight in consequence. After parturition the animal could not be reinfected; it lost steadily and at its death weighed only 410 gm., 151 days after the first treatment.

The post-mortem showed considerable emaciation, in the abdominal cavity, cloudy hemorrhagic fluid, yellow nodules covering the anterior and posterior wall; the large omentum thickened, a few nodules in the mesocecum in the mesoovarium and ligamentum latum; the kidneys pale and anemic without any tubercles on the surface nor on section. The suprarenal glands enlarged, a few gray yellowish nodules on the mesentery, liver studded with tubercle, areas of anemia on the surface and on section. Many small tubercles on the surface and on section of spleen, general hyperemia of the organ. Diaphragm presents several nodules on both aspects especially on the abdominal side, surface thickened and granulated; several tubercles in the mediastinum, on the right ventricle one yellowish white nodule noticed. Lungs, lower lobe studded with tubercles, involvement was marked in the upper lobe.

Guinea-pig No. 12. Weighed 455 gm. when first injected; after a small loss during the first three weeks the animal surpassed its initial weight; 32 days later when the first infection with .01 gm. bovine tubercle bacilli took place the animal lost in weight during the first four weeks, became pregnant, after the full term the animal lost again, dropped down to 370 gm., three months after reinfection it gained again, became pregnant, which pregnancy reached its term, then the animal declined rapidly and died 218 days after the first treatment, 172 days after the reinfection, total loss in weight amounted to 35 gm. compared with its initial weight.

The post-mortem of the animal showed enlarged inguinal glands, enlarged mesentery glands, peritoneum free from tuberculosis, spleen contains many tubercles and a few tubercular infarcts. Liver enlarged with fatty degeneration, anemic discoloration shows a few miliary tubercles, diaphragm shows two white nodules; kidneys free, lungs small miliary tubercles with more involvement of the left lung, enphysema, intestines and stomach are free from tuberculosis.

From this series of experiments with bovine tubercle bacilli it would seem that these animals are more susceptible to the disease; even if the animals survive the first treatment, they succumb to the infection at an earlier period. Pregnancy and weakening seem to have a predisposing rôle. The animals with 50 and 70% bovine bacilli died even earlier than those treated with bovine 37%+ lecithin.

In previous series with human tubercle bacilli in most instances two reinfections brought fatal results, and in the bovine series one reinfection was sufficient to develop a fatal tuberculosis. The non-reinfected animal (No. 11) finally died, although it outlived the control for a considerable time and showed a considerable outspread of tuberculosis. In one instance no tubercle lesions were found (No. 8) but it cannot be denied that in 77 days after the first treatment, and 30 days after the reinfection, death occurred as a consequence of the treatment.

Since these experiments were started (January, 1911) several reports have been published upon the favorable influence of the immunizing effect of lecithin and allied substances upon tubercular infection. So Ditthorn (*loc. citat.*) in his experiments with neurin was unable to produce experimental tuberculosis in guinea pigs without any trace of that disease nine weeks after infection. He at the same time noticed the production of complement-binding substances in the blood serum against tuberculosis, and the bacilli treated did no more develop upon the ordinary media used for such purposes. Meyer (*loc. citat.*) in his experiments noticed that antibodies were present, but that they were of a much milder action than those resulting from the treatment with the proteid antigens of

the tuberculous virus. Momose (*Deut. med. Wochenschr.*, No. 22, 1913; *Muench. med. Wochenschr*, 1913, No. 23, p. 1283) noticed that the animals were more resistant against tubercular infection. Perhaps we may be permitted to quote the impression of Deycke and Much and Leschke, who think that lecithin, neurin, cholin may exert such a destructive influence upon the tubercle bacillus, that the other antigens freed from the bacillus and of a more delicate nature may be destroyed by that treatment, so that only a partial immunity may be started, which at further infection may not be efficient enough to fight the new bacillary invasion. Although we are aware that the present observations are only a small contribution to the present problems of immunization, which of course requires more extensive animal experiments, we believe that the human tubercle bacilli are more accessible to attenuation than the bovine type, as observed from the stained preparations and from the course noted in the infected guinea-pigs.

NOTES ON THE SECOND ANNUAL CONFERENCE ON THE MEDICAL AND SOCIAL WORK OF THE PSYCHOPATHIC HOSPITAL, BOSTON, MASSACHUSETTS.

(*Concluded from page 866.*)

VIII.

VARIATIONS IN THE SENSORY THRESHOLD FOR FARADIC STIMULATION IN PSYCHOPATHIC SUBJECTS: FIRST NOTE.*

BY G. PHILIP GRABFIELD, BOSTON,

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Up to the present time our determinations of sensory disturbances have been vaguely qualitative. Through the lack of an accurate method our determinations have depended almost altogether on the intelligence and accuracy of the patient and have varied with the technic of each examiner. Dr. E. G. Martin[1] has devised a method for accurately recording the shocks delivered by the secondary coil of an inductorium by which one is enabled to check the replies of the patient and which rules out the variations in technic. The possibility of the practical application of this method was suggested by the observation that there is a constant value of the sensory threshold in normal human subjects.[2] This threshold value has been found to be in the neighborhood of 100 Beta units varying from 60 to 140 in different individuals at the same time and through a lesser range in the same individual at various times of the day. The purpose of this series of observations was merely another step in discovering the possibilities of variation in the sensory threshold, which it was hoped might be found among pathological subjects.

The quantitative method depends upon the well known fact that the strength of the "shocks" delivered by the secondary coil of an inductorium depends upon its relation to the primary coil—in this method the distance of the secondary coil from the primary on the slide on which it can be moved,—the maximum shock being obtained when the secondary is directly over the primary. The point at which the maximum shock is delivered is considered the zero position. The operator, who sits in a separate room from the patient to be tested, begins with the coil at a point where it will deliver the minimal shock and gradually moves the secondary towards the primary, breaking the current at short intervals. The patient places the second and third fingers of his left hand into two electrodes, which consist of two tubes containing 15% salt solution overlying a small layer of mercury, which lies in contact with two platinum electrodes connected with the secondary of the coil. He is instructed to press a telegraph key whenever he feels a pricking sensation in the fingers tested. This signals to the operator. As soon as the patient has signaled, the operator throws 10,000 ohms resistance into the secondary circuit and again approaches the zero position until the patient signals. This is repeated with 20,000 and 30,000 ohms in the secondary circuit, thus obtaining four readings of the position of the secondary of the coil. The resistance of the patient's skin is taken as 2100 ohms, as repeated observations have shown that this is almost constant. The resistance of the coil itself is 2900 ohms, making the four readings with the five, fifteen, twenty-five and thirty-five thousand ohms in the secondary circuit. The primary current used was 0.3 amperes. From the above data the absolute value of the threshold stimulus in Beta units is derived by certain formulae. The operator has a definite check on the patient, as he can try and retry any position to make sure that the patient is responding properly. The responses even from the psychopathic individual are remarkably constant.

In this series we have obtained 196 observations on 135 cases selected at random from the admissions to the hospital. The purpose of this series was to determine whether the quantitative method can be applied to practical psychiatry. The cases naturally fall into certain large groups, together with a large number of scattering observations on single cases.

* Being Contributions from the Psychopathic Hospital, Boston, Number 58 (1914.24), read at the Second Annual Conference on the Medical and Social Work of the Psychopathic Hospital, Boston, June 26, 1914. (*Bibliographical Note.*—The previous contribution, Number 57 (1914.23), was by Robert M. Yerkes and J. W. Bridges, entitled "The Point Scale: A New Method for Measuring Mental Capacity," published in the BOSTON MEDICAL AND SURGICAL JOURNAL, Vol. clxxi, No. 23, December 3, 1914.

	Cases.	B Units.
Delirium tremens	20	235
Acute alcoholic hallucinosis	8	158
Korsakoff's psychosis	4	405
Unclassified alcoholic	8	285
Dementia precox:		
Hebephrenic	2	760
Catatonic	8	232
Paranoid	8	131
Other forms	6	191
Syphilitic cases	13	192
Unclassified	18	219
Defective	7	189
Manic depressive insanity:		
Manic phase	5	127
Depressed phase	4	190
Neurasthenia, psychoneurosis, etc	8	120
Senile and presenile	5	314
Epilepsy	4	138
Huntington's chorea	2	308
Hypopituitarism	1	125
Hyperthyroidism + alcohol	1	183
Drug psychosis	1	158
Involutional psychosis	1	233
Normal, not insane	4	103
The average of all observations		223
Number of patients whose test proved invalid	4	
Patient whose threshold was above the calculable value	1	

In general, then, the threshold of the psychopathic individual tends to be high. As to what shall be considered a pathological threshold it is very difficult to say. Any figure must be arbitrary. Any figure over 175 is definitely pathological as far as present experience with normal thresholds has shown. A threshold that on repeated observation is over 140 is probably pathological, though such a value would necessarily mean very much less than the higher figures. It is to be remembered that we are compelled to test many of our cases after partial recovery. Of course, in the thresholds between 140 and 175, the higher the value the greater is the probability of it being pathological. It is a significant fact that we have remarkably few observations under 100 B units, in marked contrast to a similar series on normal subjects. In the total number there are only 23 such observations. Two patients answered so irregularly or had such high thresholds that the value could not be determined.

Alcohol appears to be a definite factor in raising the threshold. In the 40 cases of alcoholic psychoses of various types, the average threshold was found to be 252,—higher by 29 B units than the average of the total number of observations. The highest of this group is found to be the cases of Korsakoff's psychosis, the lowest the acute alcoholic hallucinoses. The former group show a tremendous variation,—as is to be expected. In this group, we have comparatively many observations on a few cases. These observations are absolutely irregular, but apparently consistent with the clinical picture. The acute hallucinoses, on the contrary, show much less variation, being in the doubtfully pathological class but none the less always high.

The most interesting results were obtained in the series of 20 cases of delirium tremens. In this series the average was 235, ranging from 85 to 493. Only 7 observations in this series were found to be under 200, and these were, in every case, late in the course of the disease. One case in this series was tested two days after admission and responded so irregularly that the determination was impossible. One week later, ten days before discharge, this same patient had a threshold of 129. This is a fair example of how the thresholds varied with the second and third observations on these cases. The lowest threshold of this series (85) is interesting in view of the fact that this patient was also taking morphine. The highest threshold of the series was taken on the day of admission. One case of senile dementia that was also alcoholic, showed a high threshold when first tested. This value came down to the level of the other senile cases after a short stay in the Hospital, in other words, after withdrawal of the alcohol. A similar result was obtained with one alcoholic case of dementia precox. Such results are obtained with every alcoholic case except the Korsakoff cases. In other words, the longer after the withdrawal of alcohol the threshold was tested, the nearer normal it became.

The 21 cases of dementia precox showed an average threshold of 232. Upon analysis, one very interesting fact is evident: Contrary to expectation, the catatonic form shows an average threshold of only 232 as against 760 for the hebephrenic form. The paranoid form shows a normal threshold of 131, while the remaining types show an average of 191. Thus we find in this series that paranoid dementia precox shows a normal threshold, whereas all the other forms show an abnormal threshold.

The cases of manic-depressive insanity fall naturally into two groups. As is to be expected, the patients in the manic phase show a distinctly lower threshold than those in the depressed phase, the former averaging well within normal limits, the latter being definitely pathological. One very interesting case, first observed two years ago at the end of a depression, showed at that time a threshold of 318, which gradually came down to 106 as the depression wore off. Recently he has returned, complaining of the same symptoms of depression, lassitude, loss of weight, etc., and his threshold was found to be 227.

The other large group of cases is, of course, the syphilitic psychoses. The results in this group are absolutely inconclusive. The variation is tremendous and no correlation is possible. The average is again found to be high (192).

The group of psychoneuroses show a normal threshold in every way. The percentage of those under 100 B units is higher than any other group and is practically that found in normal human subjects. The only high threshold in this group is in a case in which the diagnosis is doubtful.

In the unclassified cases the variation is naturally very great, but here again we find a general tendency to high values. Again in this group, the cases with which the use of considerable alcohol is associated show a high threshold.

The senile dementias show a definitely pathological threshold, the highest being found in an alcoholic, before mentioned.

The epileptic cases are found to have a normal threshold, as do the remainder of the cases which we have tried, with the exception of two cases of Huntington's chorea and one involutional psychosis.

Three cases showed a difference between the reflexes on the two sides. In each of these the threshold was found to be distinctly lower on the side upon which the reflexes were livelier. This is rather significant evidence about the nature of the threshold we are determining. Just which of the many possible thresholds this method determines has never been worked out. It is our hope to test a case in which the sensory impulses are dissociated and so procure more evidence on this point.

No other correlations than those heretofore mentioned are evident in this series. We have attempted to work out such correlations with blood pressure, pupillary reactions, hallucinations, delusions, emotional tone, and orientation. A depressed patient appears to have a high threshold, but many patients who are not depressed or even euphoric have as high or higher thresholds.

We have, then, merely accumulated evidence to show that the quantitative method provides a means of determining a sensory threshold in psychopathic individuals, that these individuals show a decided tendency to have a higher threshold than normal subjects, and that the excessive use of alcohol appears to exert a definite influence in raising the sensory threshold. Clinically, this method appears to have a certain value in demonstrating improvement or recovery in certain cases, especially the alcoholic psychoses. It is possible that we may find in this method a means of accurately determining the difference between the reflexes of the two sides when such difference exists. Many more data will have to be gathered before any definite conclusions can be drawn. This series, however, seems to show that conclusions of practical and scientific value can be arrived at from further work and that the determination of the sensory threshold by the quantitative method will find a place in psychiatric and neurological examinations.

CONCLUSIONS.

1. The new Martin test (1908 *et seq.*) for variations in the sensory threshold for Faradic stimulation has been used in an orientation study upon 135 psychopathic subjects, ranging from the psychoneuroses to cases of coarse brain disorder. Repeated observations have been made in many cases.

2. The Faradic threshold in psychopathic subjects of almost all kinds tends to be high, and in fact averages 223 Beta units, as against 140, considered to be the highest range of normal subjects under ordinary circumstances, and 175, considered to be definitely pathological.

3. The average threshold for alcoholic cases was 252, and among alcoholic cases the polyneuritic or Korsakoff cases ran highest.

4. Upon withdrawal of alcohol and in convalescence the threshold falls, and the method may even have practical value in gauging the degree of progress toward recovery in the delirium tremens group.

5. Interesting figures are available for cases of dementia precox, indicating that the paranoidal forms have a normal threshold, whereas those classed as catatonic and hebephrenic have pathologically high thresholds. It is remarkable that the hebephrenic cases tested (two in number) showed some of the highest thresholds calculable (760). Eight catatonic cases averaged 232 (paranoid 131).

6. The manic phase of manic depressive insanity shows a normal threshold, the depressive phase a pathologically high threshold. One case observed at intervals for two years seems to show a high threshold ranging down to normal with the variations of his depression down to a normal emotional state.

7. Beyond a high threshold average, it is impossible to ascribe to the syphilitic group more than a tremendous variation in different cases.

8. The psychoneurotics seem to have normal thresholds,—hence there may be an immediate practical value diagnostically, when the diagnosis is in doubt as against the frank psychoses.

9. The normal thresholds of the four epileptics tested are interesting, but further work is necessary here.

10. The field of threshold work in cases with unilateral lesion and with sensory "dissociation" has been touched merely.

11. It is in some ways to be regretted that the technic of this test is delicate and the calculations a bit tedious, so that the employment of the test outside hospitals is not soon likely to be extensive. But under hospital conditions it seems clear that this method is likely to add data of great interest and considerable practical value to the objective psychology of psychopathic patients.

REFERENCE.

[1] Martin, E. G.: American Journal of Physiology, 1908, 1909, 1910, 1911.
[2] Martin, Porter, and Nice: American Journal of Physiology, 1913.

IX.

EXPERIENCE WITH THE LANGE COLLOIDAL GOLD TEST IN 135 CEREBROSPINAL FLUIDS.

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THE Lange colloidal gold test is intended as a laboratory diagnostic method in the study of spinal fluid in cases of disease of the central nervous system. The reaction depends on the presence of an excess of albuminous material or abnormal albumen constituents in the fluid, and has its basis in the work of Zsigmondi,[1] who showed that albuminous substances may be differentiated through their reactions with colloidal gold solutions. This differentiation is due to the property, possessed by albumens in different degrees, of preventing the throwing down or "Ausflockung" (flaking out) of the gold particles by electrolytes.

In the case of cerebrospinal fluid it is found that in certain disease conditions the colloidal gold is thrown down by addition of the fluid as it would be by an electrolyte. It is known that while proto- and hetero-albumoses protect the colloidal metal, that deutero-albumoses act in this respect like electrolytes. We are not prepared to draw any conclusions or comparisons, however.

Details of the technic may be found in Lange's[2, 3] original contributions or in any of the articles mentioned below. Briefly the test is performed as follows. Ten tubes are set up in a rack. To the first tube 1.8 c.c. of a 0.4% salt solution is added and to each of the following tubes 1c.c. Then to the first tube 0.2 c.c. of the spinal fluid to be tested is added, making a dilution of 1/10. From this tube 1 c.c. is pipetted into the second tube and so on to each tube, the extra c.c. from the last tube being thrown away. This gives dilutions of spinal fluid of 1/10, 1/20, 1/40, 1/80, 1/160, and so on to 1/5120 in the last tube. Five c.c. of gold reagent is added to each tube. After a number of hours the results are read.

By a positive reaction is meant a flaking out of the gold and this causes a color change which varies with the intensity of the reaction. The color changes from the original red through red blue, blue red, violet or dark blue, light blue, to clear, and the color changes are represented by 1-5 plusses.

By charting these results and comparing them with the clinical and laboratory knowledge of the cases, certain conclusions have been offered by several workers. It is claimed that the reaction will in general give a characteristic curve in syphilitic disease of the central nervous system, differing from that found in the septic meningitides and in at least some cases of tubercular meningitis, and that non-inflammatory disease will give a negative test. Syphilitic disease gives a reaction in the lower dilutions, that is, the color change is most marked in the tubes with dilutions from 1/10-1/160. General paresis characteristically gives a "Five" reaction beginning on the first tube and running through a number. Tabes and cerebrospinal syphilis give weaker reactions and usually do not give as strong reactions in the first tube as in the second or third. The septic meningitides give strong reactions running through the middle and high dilutions. Tubercular meningitis tends to cause the reaction in the high dilutions.

Reports of the test have been given by Lange,[2, 3] Jaeger and Goldstein,[4] Eicke,[5] Grulee and Moody,[6] Sippy and Moody,[7] Kaplan and McClelland,[8] Kaplan,[9] Miller and Levy,[10] Lee and Hinton.[11] As our evaluation of the test must depend upon a comparison of results where the diagnosis is fairly substantiated by other tests or by autopsy, we are giving our results in full with the clinical diagnosis, the Nonne test for globulin, the Mestrezat test for albumen, the cell count and the Wassermann reaction in serum and fluid. (Wassermann reactions marked "c" mean positive only with cholesterin-reënforced antigens.)

It will be seen from Table I that the cases of general paralysis give fairly constant and characteristic reactions. There are 25 cases with 28 spinal fluids diagnosed from the clinical and laboratory findings as general paralysis or cerebrospinal syphilis. The characteristic paretic reaction, *i.e.*, 5 plus change beginning in the first tube and continuing through a number of dilutions was typically given in 20 cases.

Of the five atypical reactions, one, L. M., No. 96, is very suggestive, and the fluid taken again two weeks later, during which time four intravenous injections of salvarsan were given, is quite typical. This case is not a typical general paretic. The symptoms are optic atrophy of about two years' duration, paralysis of one external rectus, nystagmus, ankle clonus and very little if any mental change. The second case, J. R., No. 114, giving a very slight reaction, was under salvarsan therapy and has shown a remission of mental symptoms and the laboratory signs have all returned to near normal. The third atypical result is in the case of A.De., No. 140, with ten cells per c.mm., and Wassermann

* Being Contributions from the Psychopathic Hospital, Boston, Number 59 (1914.25), read in abstract at the Second Annual Conference on the Medical and Social Work of the Psychopathic Hospital, Boston, June 26, 1914. The sincere thanks of the writers are given to Dr. H. M. Adler for permission to carry out these tests, most of which were executed with Psychopathic Hospital material. Thanks are also due Dr. I. C. Walker of the Peter Bent Brigham Hospital who courteously furnished them with several fluids. Certain tests marked X were performed at the Psychopathic Hospital by Drs. Ward H. Cook and Ivan R. Burkett, whom the writers wish to thank also. (*Bibliographical Note.*—The previous contribution, Number 58 (1914.24), was by G. Philip Grabfield, entitled "Variations in the Sensory Threshold for Faradic Stimulation in Psychopathic Subjects: First Note," published in the BOSTON MEDICAL AND SURGICAL JOURNAL, Vol. clxxi, No. 24, December 10, 1914.

TABLE I. GENERAL PARALYSIS, CEREBROSPINAL SYPHILIS AND CEREBRAL SYPHILIS.

Name.	No.	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
E. G.	11	5	5	5	5	5	4	3	1	0	0	+	+	35	+	+	G. P.
W. R.	12	5	5	4	4	3	3	2	1	0	0	+	+	27	+	+	G. P. or C. S. S. (treatment)
"	70	5	5	5	5	5	5	4	3	0	0	+	+	+	+	+	One week later "
"	97	3	3	5	4	4	4	2	1	0	0	+	+	+	+	+	One month later "
G.	13	5	5	5	5	5	3	1	0	0	0	+	+	35	+	+	G. P.
F. K.	15	5	5	5	5	5	3	1	0	0	0	+	+	37	+	+	G. P.
R. D.	32	5	5	5	5	5	5	4	3	2	0	+	+	135	+	+	G. P.or C. S. S.
A.	55	5	4	4	4	4	4	3	3	3	0	+	+	+	+	+	G. P.
C.	75	5	5	5	5	5	5	4	3	1	0	+	+	113	+	+	G. P.
J. H.	95	5	5	5	5	5	5	5	5	1	0	+	+	29	+	+	G. P.
A. D.	119	5	5	5	5	5	5	5	5	3	1	+	+	225	+	+	C. S. S. or G. P.
C. D.	130	5	5	5	3	3	2	0	0	0	0	+	+	67	+	+	Taboparesis
M. O.	149	5	5	5	5	5	5	4	2	1	0	+	+	13	+	+	G. P.
S. S.	155	5	5	5	5	5	5	5	5	3	2	+	+	28	+	+	G. P.
A. Da.	165	5	5	5	5	5	5	2	0	0	0	+	+	41	+	+	G. P.
W. S.	166	5	5	5	5	5	5	5	4	2	0	+	+	42	+	+	G. P. or C. S.S.
C. M.	171	5	5	5	5	5	3	1	0	0	0	+	+	33	+	+	G. P.
W. D.	172	5	5	5	5	3	2	1	0	0	0	+	+	140	+	+	C. S. S. or G. P.
W. A.	204	5	5	5	5	5	4	3	2	0	0	+	+		+	+	G. P.
J. B.	201	5	5	4	4	4	2	1	1	1	1	+	+	7	+	+	G. P.
J. M.	196	5	5	5	5	5	5	5	3	1	1	+	+	44	+C	+	G. P.
P. H.	193	5	5	5	5	5	5	4	2	1	0	+	+	32	+C	+	G. P.
M.	51	0	0	0	1	2	2	1	0	0	0	0	N	0	+	—	C. S.
L. M.	96	4	4	3	1	1	2	2	0	0	0	+	+	10	—	+	C. S. S. or G. P.
L. M.	110	5	5	5	3	3	2	1	0	0	0	+	+	25	—	+	C. S. S. or G. P. Interval, two weeks
J. R.	114	0	0	1	1	1	1	0	0	0	0	+	+	4	+C	—	G. P. improved under treatment
J. A.	135	3	4	3	2	2	1	0	0	0	0	+	+	164	+	+	G. P. or C. S. S.
A. De.	140	1	1	1	1	0	0	0	0	0	0	+	+	10	+C	+C	G. P.
N. S.	24	2	1	1	3	5	4	2	1	0	0	+	+	100	+	+	G. P. or C. S. S. Repeated different reaction each time

TABLE II. TABES.

Name.	No.	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
C.	46	0	2	2	2	2	1	0	0	0	0	+	+	9	+	+	Tabes
C.	47	0	1	1	2	2	2	1	0	0	0	+	+		+	+	" Interval several days with intraspinous treatment
C.	48	0	1	1	2	2	2	1	0	0	0	+	+		+	+	"
C.	49	0	1	1	2	2	2	1	0	0	0	+	+		+	+	"
C.	50	0	0	1	2	2	2	2	1	0	0	+	+		+	+	"
S.	40	0	0	0	1	2	1	0	0	0	0	+	+	6	+	+	"
S.	41	0	0	0	1	1	1	0	0	0	0	+	+		+	+	" Interval several days with intraspinous treatment
S.	42	0	0	0	1	1	2	0	0	0	0	+	+		+	+	"
S.	43	0	0	0	2	2	2	0	0	0	0	+	+		+	+	"
S.	44	0	0	0	0	1	1	0	0	0	0	+	+		+	+	"
S.	45	0	0	0	2	2	2	1	0	0	0	+	+		+	+	"
J. C.	17	2	1	1	3	3	3	0	0	0	0	+	+	2	+C	+C	Tabes?

TABLE III. CONGENITAL SYPHILIS.

Name.	No.	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
F. M.	1	0	2	4	3	3	2	2	1	0	0	+	+	110	+	+	Juvenile paresis
F. S.	2	0	0	0	0	0	0	0	0	0	0	0	N.	0	+	—	Cong. syphilis, age 21
F. Sh.	3	0	0	1	0	0	0	0	0	0	0	0	N	0	+C	—	" " optic atrophy
E. C.	79	0	0	0	1	1	0	0	0	0	0	0	N	0	—	—	" " (?) treatment
L. N.	89	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	" " Sisters
B. N.	2x	0	—	—	—	—	0	0	0	0	0	0	N		+C	—	" "
M. N.	3x	0	—	1	1	1	1	—	0	0	0	0	N	22	+	+C	" "
G. F.	160	1	1	1	1	1	0	0	0	0	0	0	N	3	+C	—	" "
J. K.	157	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	" "
M. F.	1x	0	0	2	2	1	0	0	0	0	0	0	N	8	—	—	" "
J. Mc.	5x	0	0	1	2	1	1	—	1	0	0	0	N	0	+C	—	" "
No. 4G.	209	0	0	0	0	0	0	0	0	0	0	0	N		+	—	Syphilitic meningitis

TABLE IV. WASSERMANN REACTION POSITIVE IN SERUM OR FLUID DIAGNOSIS OTHER THAN SYPHILIS OF THE NERVOUS SYSTEM.

Name.	No.	1 10	1 20	1 40	1 80	1 160	1 320	1 640	1 1280	1 2560	1 5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
A. K.	90	0	0	1	1	1	0	0	0	0	0	0	N	2	+C	—	Chronic alcoholism
M. K.	105	1	1	1	1	2	1	0	0	0	0				+C	—	Dementia praecox
A. H.	148	1	0	0	0	0	0	0	0	0	0	0	N	0	+	—	Tertiary syphilis and dementia praecox
M. P.	150	0	0	1	1	1	0	0	0	0	0	0	N	2	+C	—	Dementia praecox
J. C.	151	0	0	1	1	0	0	0	0	0	0	0	N	2	+C	—	Defective delinquent
M. L.	173	1	1	1	0	0	0	0	0	0	0	0	N	2	+C	—	Manic depressive or dementia praecox
N. D.	176	0	0	1	2	2	1	0	0	0	0	0	N	0	+C	—	Manic depressive
G. S.	198	0	1	1	1	1	0	0	0	0	0	0	N	2	+	—	Korsakoff
J. M.	199	0	0	1	1	1	1	0	0	0	0	+	+	2	—	+C	Arterio sclerosis with cerebral hemorrhage
E. A.	4	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Dementia praecox
A. S.	16	0	0	0	0	0	0	0	0	0	0	0	N	0	+	—	Unclassified
C. A.	61	0	0	0	0	0	0	0	0	0	0	0	N		+C	+C	Chronic alcoholism
M. C.	62	0	0	0	0	0	0	0	0	0	0	0	N	0	—	+C	Dementia praecox
L. M.	63	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Anemia
M. J.	69	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Defective
C. C.	76	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	
M. K.	71	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Involution psychosis
A. S.	83	0	0	0	0	0	0	0	0	0	0	0	N		+C	+C	Syphilitic cerebral endarteritis with old hemiplegia
L. S.	84	0	0	0	0	0	0	0	0	0	0	0	±	7	+	—	Manic depressive
P. C.	91	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Defective delinquent
F. G.	92	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Unclassified
C. H.	99	0	0	0	0	0	0	0	0	0	0	0	N	0	+C	—	Epilepsy
M. S.	117	0	0	0	0	0	0	0	0	0	0	0	N	2	+C	—	Manic depressive
S. P.	118	0	0	0	0	0	0	0	0	0	0	0	N	2	+C	—	Hysteria
J. M.	133	0	0	0	0	0	0	0	0	0	0	±	+	—	+	—	Alcoholism
M. G.	131	0	0	0	0	0	0	0	0	0	0	0	N		+C	—	Dementia praecox
M. D.	139	0	0	0	0	0	0	0	0	0	0	0	N		+	—	Manic depressive
F. v. E.	141	0	0	0	0	0	0	0	0	0	0	0	N	6	+C	—	Dementia praecox
P. C.	144	0	0	0	0	0	0	0	0	0	0	0	N		+	—	Drug psychosis
C. C.	118	0	0	0	0	0	0	0	0	0	0	0	N		+C	—	Syphilitic periostitis
M. C.	127	0	0	0	0	0	0	0	0	0	0	0	+	1	+C	—	Psychasthenia
M. Mc.	23	0	0	0	0	0	0	0	0	0	0	±	+	2	+C	—	Unclassified
J. G.	205	0	0	0	0	0	0	0	0	0	0	0	N	1	—C	+	Unclassified

TABLE V. WASSERMANN REACTION NEGATIVE IN BOTH SERUM AND FLUID.

Name.	No.	1 10	1 20	1 40	1 80	1 160	1 320	1 640	1 1280	1 2560	1 5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
W. L.	30	0	0	0	1	0	0	0	0	0	0	0	N	2	—	—	Alcoholic hallucinosis
C. W.	81	0	0	1	1	0	0	0	0	0	0	0	N	1	—	—	Alcoholic hallucinosis
W. F.	194	0	0	2	2	2	1	0	0	0	0	0	N	0	—	—	Alcoholism
C. C.	197	0	0	1	2	2	1	0	0	0	0	—	+	0	—	—	Korsakoff
A. Mc.	5	1	1	3	3	2	2	1	0	0	0	+	+	6	—	—	Unclassified
M. W.	147	0	0	0	1	1	0	0	0	0	0	+	N	2	—	—	"
M. N.	18	0	0	0	0	0	1	0	0	0	0	+	+		—	—	"
C. L.	88	0	1	1	2	1	0	0	0	0	0	0	N	2	—	—	Multiple sclerosis
J. W.	111	5	3	4	3	3	2	1	0	0	0	+	+	8	—	—	" "
J. W.	192	5	5	5	5	4	3	2	0	0	0	+	+	7	—	—	" " 5 months later
W. C.	203	0	0	1	1	0	0	0	0	0	0	0	N	3	—	—	Defective delinquent
W. M.	202	2	2	2	2	2	1	1	1	0	0	0	N	0	—	—	
R. S.	31	0	0	0	1	1	1	0	0	0	0	0	+	0	—	—	Cerebral hemorrhage
J. R.	77	0	0	0	1	1	1	0	0	0	0	0	+	0	—	—	Fracture base of skull ? cerebral hemorrhage
E. B.	93	0	0	0	1	1	1	0	0	0	0	±	+	2	—	—	Mastoiditis. ? brain abscess
P. C.	106	0	0	0	1	0	0	0	0	0	0	±	+	1	—	—	Organic dementia
L. B.	109	0	0	0	0	1	0	0	0	0	0	0	N	2	—	—	Paralysis agitans
C. F.	146	2	1	1	1	0	0	0	0	0	0	0	N	0	—	—	Optic atrophy, age 15
W. R.	87	0	1	1	2	2	2	1	0	0	0	0	+	1	—	—	Epileptic deterioration
M. C.	159	1	1	1	1	1	0	0	0	0	0	0	N	1	—	—	Dementia praecox
J. A.	7	0	0	0	0	0	0	0	0	0	0	0	+	3	—	—	Chronic alcoholism
H D.	14	0	0	0	0	0	0	0	0	0	0	0	±		—	—	Delirium tremens
J. B.	20	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Alcoholism and paraphrenia
O'C.	102	0	0	0	0	0	0	0	0	0	0				—	—	Alcoholism and feeble-minded
McG.	103	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Delirium tremens
J. G.	110	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Alcoholism

TABLE V.—(*Continued.*)

Name.	No.	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
J. L.	121	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Alcoholic hallucinosis
A. Y. .	138	0	0	0	0	0	0	0	0	0	0	0	N	3	—	—	Alcoholic hallucinosis or dementia praecox
T. D.	167	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Delirium tremens
W. H.	206	0	0	0	0	0	0	0	0	0	0	+	+	2	—	—	Alcoholism
C. K.	122	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Dementia praecox
M. F.	128	0	0	0	0	0	0	0	0	0	0	0	N		—	—	" "
J. B.	132	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Dementia praecox or manic depressive
A. L.	134	0	0	0	0	0	0	0	0	0	0				—	—	Dementia praecox
L. B.	113	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Manic depressive
J. V.	6	0	0	0	0	0	0	0	0	0	0	0	+	3	—	—	Unclassified
E. L.	9	0	0	0	0	0	0	0	0	0	0	0	N	2	—	—	"
J. F.	18	0	0	0	0	0	0	0	0	0	0	±	N	1	—	—	"
J. M.	78	0	0	0	0	0	0	0	0	0	0	0	N	2	—	—	"
J. H.	80	0	0	0	0	0	0	0	0	0	0				—	—	"
C. H.	104	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	"
C. G.	123	0	0	0	0	0	0	0	0	0	0	±	N	0	—	—	"
J. L.	158	0	0	0	0	0	0	0	0	0	0	0	N	3	—	—	"
C. J.	8	0	0	0	0	0	0	0	0	0	0	0	N	2	—	—	Multiple sclerosis
F. H.	21	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Hypopituitarism
A.	52	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Serous meningitis
L. C.	53	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Echinococcus cyst
V. Y.	72	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Nervous
J. P.	107	0	0	0	0	0	0	0	0	0	0	0	—	4	—	—	Cerebral hemorrhage
W. M.	108	0	0	0	0	0	0	0	0	0	0	0	N	2	—	—	Imbecile
K. M.	129	0	0	0	0	0	0	0	0	0	0	0	N	2	—	—	Sex pervert
P. F.	136	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Organic dementia
N. S.	189	0	0	0	0	0	0	0	0	0	0	0	N	0	—	—	Hysteria
No.SY.	208	0	0	0	0	0	0	0	0	0	0	0	N		—	—	Brain tumor

TABLE VI. TUBERCULAR MENINGITIS.

Name.	No.	1/10	1/20	1/40	1/80	1/160	1/320	1/640	1/1280	1/2560	1/5120	Glob.	Alb.	Cells.	W. R. Ser.	W. R. Fl.	Diagnosis and Remarks.
B.	54	0	0	0	0	1	2	3	3	2	0	+	+	500	+	+	Tubercular meningitis
C.	101	0	0	0	0	1	2	2	1	0	0	+	+		+	+	Miliary tuberculosis
M. M.	88	0	0	0	1	3	2	0	0	0	0						Ventricular fluid P.M. Tubercular meningitis
In.	208	0	0	0	0	0	1	2	2	1	0	+	+		—	—	Tubercular meningitis

reaction in serum and fluid positive only with cholesterin reënforced antigens. The fourth case, J. H., No. 135, may be either paresis or cerebrospinal syphilis from the clinical picture. The fifth case for some unknown reason in five trials gave different results each time.

As we are not certain in many of these cases whether the diagnosis is paresis or cerebrospinal syphilis, we are unable to draw any conclusions from these tests as to the value of the method in differentiating the two. Only further experience with autopsy check will tell us. One case with the clinical diagnosis of cerebral syphilis gave a reaction typical of syphilis and differing markedly from general paresis.

The fluids from the three cases diagnosed tabes dorsalis give reactions very different from the paretic fluids. They are particularly interesting in that the fluids were obtained at short intervals during intraspinous treatment, and that the result of each test is so similar to the preceding test.

In order to test the effect of salvarsan injected in this way into the spinal canal, amounts of salvarsan somewhat in excess of the amount injected by the intraspinous method were added in vitro to the gold reagent. A reaction occurred, but if spinal fluid from a normal case in any dilution up to 1/5120 were added it served to protect the reagent and no color change occurred.

As the intensity of the color change has been reported to become less as a patient improves under treatment from paresis and tabes, we attempted to see if there were any differences in the reactions that could be looked upon as indicative of the severity of the process. The fluids were tested in dilutions of 1/1, 1/2, 1/4, 1/8, and also compared at the other end of the scale, but no general relation was found in these reactions either as to the duration of the disease or the clinical symptoms.

Of the twelve cases of congenital syphilis, only one gave a marked reaction and that a case of juvenile paresis. The diagnosis in each case was made with the aid of the family study. These results are quite different from those reported by Grulee and Moody, as they got fairly

marked reactions in nine of ten cases, but all their patients were under six months of age, while ours ranged from three years to over twenty years of age. An interesting result is obtained in the case of M.F., No. 5x. This child aged four, of syphilitic parents, born while mother was under anti-syphilitic treatment, is unable to talk, or feed itself, is barely able to walk, shows athetoid-like movements and general mental deficiency. With the exception of a border line number of cells in the fluid all tests except the colloidal gold are entirely negative, and yet it seems that there can be little doubt but that the child is syphilitic.

There are 33 cases giving positive Wassermann reactions which are diagnosed as other than syphilis of the central nervous system. Of these, 10, or 30.3%, give some reaction in the syphilitic zone, mostly very slight. At first sight this would seem to suggest that we here have an important indication of the involvement of the central nervous system by the syphilitic virus. But when we find that of the fifty-three cases giving a negative Wassermann reaction and no other indication of syphilis, 18, or 33.9%, give reactions mostly in the syphilitic zone, the validity of the former assumption is shaken. A number of these latter cases show increase in globulin and albumen by other tests, so it is to be expected that a reaction would occur with the gold reagent. It is possible in the cases that show no reaction with the cruder tests that the colloidal gold gives us a more valuable test for the presence of abnormal substances.

Of the non-syphilitic cases the case of mutiple sclerosis, J. W., Nos. 111 and 192, gives a reaction such as is characterisitic of paresis. Kaplan and McClelland have reported a similar finding. A second case of multiple sclerosis gives a reaction in the syphilitic zone, while a third case is quite negative.

Very interesting is the case of C. F., No. 146, whose gold reaction is suggestive of syphilis. The patient is aged 15. He has had optic atrophy since the age of 5 of no known etiology. There is marked nystagmus, paralysis of one external rectus, no reaction of the pupils, absent abdominal reflexes, knee jerks and ankle jerks obtained only on reënforcement. Patient is feeble minded and recently has had attacks of *petit mal*. The clinical diagnosis of syphilis was made, but all tests for syphilis are negative. The father denies infection and gives a negative Wassermann reaction, as does the patient's brother.

Four cases of tubercular meningitis gave reactions not to be confounded with syphilitic disease, as the change takes place in the higher dilutions. Two of these cases are of extreme interest in showing the great value of the test. B. No. 54, presenting the clinical picture of a terminal stage of general paresis; serum and spinal fluid positive by the Wassermann test, globulin increased and 500 cells per cmm. in the fluid, was given intraspinous treatment with the result that the cell count fell rapidly but the patient died. Autopsy and inocualtion showed this to be a tubercular meningitis. A second case 6, No. 101, with an almost identical clinical picture and laboratory findings showed at autopsy miliary tuberculosis with involvement of the brain. The ventricular fluid obtained post mortem gave a reaction similar to the other tubercular fluids. It would seem then that in these two cases the colloidal gold test was the only one of any real diagnostic value.

CONCLUSIONS

1. The test requires very small quantities of fluid, is rapid, easy and cheap, but must be done with great care.

2. Paresis gives very typical reactions, but cases of undoubted paresis may give atypical reactions, and cases not paresis may give the type reaction.

3. We are unable to offer any conclusion as to its value in the differentiation of cerebrospinal syphilis and paresis.

4. Tabes gives a reaction quite different from paresis, fairly characteristic of syphilis, but not in itself diagnostic of tabes.

5. It is of no certain value in cases of congenital syphilis showing no other signs of central nervous system involvement.

6. Non-syphilitic cases give at times reactions in the so-called syphilitic zone.

7. In view of the above statement it can be maintained that, a reaction in the syphilitic zone in cases of syphilitics does not necessarily argue syphilitic involvement of the central nervous system, all other signs being negative.

8. It would seem to offer a differentiation of tubercular meningitis, and is here at times more valuable than any other test.

9. New avenues of speculation and investigation are opened which must lead to increased knowledge of the spinal fluid and other body fluids through their reactions with colloidal solutions.

10. We feel that it is a most valuable and important addition to our laboratory equipment of diagnostic aids.

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X.

Cases to Illustrate Symptomatic Psychoses of Cardiorenal Type.*

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It is becoming more and more clear that we cannot trust entirely to purely clinical pictures for the diagnosis of mental diseases. It is well known that the Kraeplinian diagnoses dementia precox and manic-depressive insanity are hardly to be so easily differentiated as it seemed when these diseases were first formulated. It has often been shown that general paresis is a disease which cannot be safely diagnosticated from the mental symptomatology and that even the characteristic neurological symptoms of general paresis are not entirely pathognomonic.

Study in psychiatric clinics and psychopathic hospitals of the so-called *symptomatic psychoses* is aiding in the above-mentioned tasks of differential diagnosis. Certain cases belonging in the group of symptomatic psychoses markedly simulate such conditions as manic-depressive insanity, dementia precox, various alcoholic psychoses (including Korsakoff's psychosis) and even general paresis. The following paper presents a brief clinical analysis of certain cases of the group. The chemical side of these other groups of mental disease is being investigated upon the more modern lines by Dr. H. M. Adler,[1] whose first publication on the topic appeared in The Boston Medical and Surgical Journal as Psychopathic Hospital Contribution No. 50 (1914.16). Credit is hereby given Dr. Adler for suggestion of this topic of investigation, and the names of the physicians and internes who have carried out the tests are given below.

Mentally, in these groups of cases are found disorders of orientation, clouding of consciousness, frequently with confabulation, delusions of both a grandiose and persecutory nature, with a strong tendency towards systematization, hallucinations, frequently auditory or visual, less frequently olfactory and gustatory, disturbance in the fields of association, incoherence in thought, emotional instability, distinct euphoria, more or less deep depression, disturbances of judgment and will, negativism, cerea flexibilitas, stupor, excitement.[2]

Neurologically, there have been observed tremor, ataxic disturbances, stumbling and hesitating speech,[3] disturbances of the cranial nerves,[2] isolated disturbances of the eye muscles,[3] paralysis of the facial nerve,[3] pupillary changes—unequal pupils and pupils which react but sluggishly and within narrow limits to light[2] or not at all,[3] tendon reflexes increased,[4] diminished or absent,[5] the presence of a Kernig,[6] and a Babinski,[3] aphasia,[7] paraplegia,[8] and hemiplegia.[9]

Bonhoeffer has termed these cases symptomatic psychoses.[2] Their etiology is frequently obscure, but they are "thought to be essentially due to certain infectious diseases, certain conditions of exhaustion, certain organic non-nervous diseases, and certain constitutional disorders."[10]

A number of these cases have passed through the hospital in the last year, and from the group I have selected two which are representative of the class and instructive because of their close similarity to other conditions.

Case 1. No. 3042. Male. Age, 16 years. Nothing is known of the family except that the mother has been committed three times with a diagnosis of manic-depressive insanity.

Previous History of Patient. Always rather morose, solitary, and totally lacking in courage. Never well nor strong. Of an introspective, melancholy temperament. Two years ago, while carrying a heavy basket, had a sudden pain in his back and testicles and thought he "had ruptured himself." He ascribes all his illness to this, and says that he has never been well since. In March, 1913, was told he had kidney trouble and was sent to a hospital for three weeks. Feet are said to have been swollen at this time. Said to have been discharged fairly well. In August, 1913, feet and abdomen became markedly swollen again and he entered another hospital where he remained seventeen weeks. During that time the edema entirely cleared up, but he grew constantly weaker and steadily lost weight, weighing only seventy pounds when discharged. Until April 7, 1914, he remained under the care of his mother. He remained constantly in bed—became progressively weaker. His diet, during this time, consisted entirely of egg noggs and brandy. On April 7, had four fainting spells and was taken to a neighboring hospital where a provisional diagnosis of inanition was made, later changed to nephritis. Shortly after entrance, mental symptoms developed. The patient was seen in consultation, and the mental study then begun was continued at the Psychopathic Hospital after the patient's transfer on June 6, 1914.

Mental Condition. There were periods of excitement alternating with stupor. When in stuporous condition, could occasionally be aroused to give name, age, and address, but that was all. Usually did not attend to questions. During the periods of excitement, attention could seldom be gained. Visual hallucinations were present. Spontaneous speech was rambling in character, loose in construction, more or less incoherent, and had to do with his hallucinations and various plans on going home; was frequently negativistic; exhibited marked cerea flexibilitas at times. Frequently had to be fed. Soiled. Had one to two clonic convulsions almost daily. Mental diagnosis previous to entrance: catatonic dementia precox.

Physical Condition. Inspection suggests that the patient is suffering from some severe constitutional disorder. Skin is sallow, pale, and very edematous,

* Being Contributions from the Psychopathic Hospital, Boston, Number 60 (1914.26), read at the Second Annual Conference on the Medical and Social Work of the Psychopathic Hospital, June 26, 1914. (*Bibliographical Note.*—The previous contribution, Number 59 (1914.25), was by H. C. Solomon and H. O. Koefod, entitled "Experience with the Lange Colloidal Gold Test in 135 Cerebrospinal Fluids," published in the Boston Med. and Surgical Journal, Vol. clxxi, No. 24, December 10, 1914.

eyelids swollen. Feet and ankles are markedly swollen. Fluid in the flank. Heart not enlarged; soft systolic murmur at apex. Pulse weak, but regular. Lateral nystagmus. Biceps, triceps, abdominal, cremasteric patellar, Achilles reflexes not obtained. No Babinski, Gordon nor Oppenheim reflex.

Blood Examination. Hemoglobin 80%, R. B. C. 4,000,000, W. B. C. 20,000, Neutro. 91½, large mono. 5%, small mono, 4%, reds not remarkable. The leucocyte count fell gradually in the course of a few days to 10,900.

Urine Examination. A series of urine examinations showed specific gravity varying from 1010 to 1016—small amounts of albumen, a few hyaline casts, granular casts fairly abundant.

Renal Function Tests. (1) 1 hr., no specimen; 2 hrs., 30%. (2) 22%, 25%—47% total. (3) 41%, 22%—63% total.

Chemical Study of Blood. A series of examinations showed; 37 mg., 30.1 mg., 31.6 mg., 27.7 mg. per hundred cc. of non-proteid nitrogen.

CASE 2. No. 12,810. Male. Age, 52 years. Contractor and builder. Family history negative except that mother, who died at 77, was rather childish during the latter years of her life, and a sister died at 48 of uremic poisoning.

Mental Makup and Character. Very cheerful; no depression; social, never seclusive. Even-tempered. Fond of his home. Somewhat demonstrative. Reserved, in general. Self-reliant. Got on well with people. Widely interested. No alcohol. No tobacco, except rarely a cigar. No drugs. Married. Married life very happy. Children: A son 25, who at one year had one convulsion, followed by what the physician called "hysteria"; a son 9, always well; no miscarriages. Life has been uneventful. Has been prosperous.

Medical History. Not known to have had any venereal disease. Typhoid fever 19 years ago. In earlier years, somewhat subject to headaches and vomiting. About 6 years ago, applied for life insurance and was rejected because of "too much albumen in the water." At that time, was advised to diet, but did not do it. Last winter had a mild attack of whooping cough.

Present Illness. Informant (wife) dates present trouble from August, 1913. At that time patient was in Baltimore in exceedingly hot weather. Took several cold baths each day; when he returned home he had severe headache and complained of not feeling well; was thought to have gout. In September, had slight frontal headache, and continuous nausea, without vomiting. Dr. C. was consulted. In October, patient went to Philadelphia on business, and while there became worse, without much change of symptoms. Came home with "high fever." Consulted Dr. H. who told him, informant says, that he had enlargement of the prostate gland, which would sometime require an operation of so serious a nature that not more than one out of a hundred survived. After this, the patient seemed worried, and immediately began to talk about his financial affairs, and to make arrangements as if he expected to die. At about this time, he was in bed for two weeks, with some fever; was very sleepy. Finally got better and was able to do some work. He then made a claim on the Health and Accident Association (in which company he is insured) for his illness. This necessitated a medical examination, and Dr. H. was sent by the company for the purpose. Dr. H. gave the patient medicine, which, informant says, proved to be "regular dope." He took the medicine for at least two weeks, and during that time would sleep almost continuously from 20 to 24 hours. In February, Dr. L. was called. He found a slight trace of albumen in the urine. At this time, patient was in the house for five weeks, but not on a diet. At the suggestion of Dr. L. in February, Dr. V. was consulted, who said there was slight kidney trouble, but found nothing serious. The blood pressure was said to be practically normal. Lost his sexual power a year and a half ago. Has drunk large quantities of water for some time, as many, sometimes, as eighteen glasses within an hour. Incontinent urine. In November, 1913, began to be extremely irritable; continually found fault with the behavior of his younger child. Began also, to be very small about money matters. Wanted to save. After giving his wife an allowance, would charge against her account any trifle he bought for her. Then again at Christmas time became very generous. Until within a month, there have been no tremor, no speech defect, no convulsions. Loss of memory has been evident for some months. About three weeks ago, his speech became thick, and at about the same time he began to drag his feet. At times has not known his wife. Said that his mother (who is dead) had visited him; that he had talked with her and with his sister and brother. Has had considerable time disorientation. Made meaningless movements. Dressed and undressed several times when getting ready for bed. For about ten days has been unable to see; walks like a blind person. A day or two ago got down on the floor to look for a glass. Occasionally had clearer periods when he knows what he has been doing.

Mental Examination. When visited on ward rounds the morning after admission, patient recognized the chief-of-staff, whom he had known well during the early days of the hospital.* He knew where he was and remarked that he had never expected to be a patient in this hospital. Later in the day, he became excited and tore his blankets and sheets into strips; soiled the floor. The strips of blanket and sheet he tied about his feet in a fantastic manner. When visited, he was found without clothing, wandering about the room, evidently much confused. Asked why he had so bundled up his feet, remarked that he had walked so fast he had frozen them. He was oriented for person. The time he gave as March, 1915; place as the Naval Hospital, Philadelphia. Asked if he were not in the Psychopathic Hospital, said no—that the Psychopathic Hospital was a part of the Naval Hospital, but was located on the corner of Broad and Main Streets, while this hospital was on Susquehanna and Broad. When asked the name of the building across the way (House of the Good Shepherd), said it was the Psychopathic Hospital and that he built it.

There was marked loss of memory for both remote and recent times. Gave the year of his birth as 1814, his age at 34; date of his marriage as June 23, 1914; named his children incorrectly. Remembered the names of the architects who drew the plan for the Psychopathic, and the approximate cost of the building, but could recall practically no other detail of the building. At times said he had finished the building six months ago, at other times that it was not yet finished. Could not name the superintendent, the director, nor the chairman of the Board of Trustees. When the various names

* Patient was closely associated with the building of the Psychopathic Hospital.

were given to him, he did not place them correctly. The gaps in his recent memory he filled with fabrications.

Q.—When did you come to the hospital? A.—I just arrived this morning. (Had come the day before.) Q.—Who came with you? A.—I came by myself. (Was brought by his son.) Q.—What are you doing here? A.—Why I came to look after the construction and the dedication. Q.—But why haven't you your clothes on? A.—Well, they took them away from me. Q.—Why was that? A.—Well, there was a question about the broken bones. Q.—What bones? A.—A bone in my leg. Q.—Which leg? A.—One of the laborers,—then the question of my sickness came up; the doctor wanted to know about the blood on the floor. I told him I had been having a nose bleed. He said, "Well, you must have bled quite a bit." I said yes, a good deal. Then he wanted to know how long that had been going on, and I said, well, for quite a time, ever since I started to construct the building; I've been bleeding from the nose and the mouth quite a bit, oh, for four or five years, I guess. Q.—What was the name of the doctor who saw you? A.—Oh, Dr. Chase, wasn't it? No, I think it was Dr. Channing. Q.—Where did you spend last night? A.—Well, I was stopping with friends in town. Q.—With whom did you have your supper? A.—With Dr.—oh, that's funny, I can't think of his name; the girl's father that died. Q.—When were you in Boston last? A.—Oh, about two months ago. Q.—Did you say you just came this morning? A.—Yes, I just arrived; I'm going out tonight.

He thought the examiner was a reporter and spoke of an article describing the hospital, which he said was in the morning's paper. Said the reporter was up to see him yesterday and he gave him an account of the building and let him take some pictures.

Has delusions of grandeur. Says he built all the buildings around here. Magnifies considerably the amount of his wealth, the number of his servants, and automobiles. Says he does not own an aeroplaine, but rents one occasionally as he needs it.

Definite evidence of hallucinations has not been obtained.

Emotionally,—he is self-satisfied, contented with his surroundings, slightly euphoric. Is restless; keeps walking about and busies himself picking up small things; such as lint, about the room.

Since this examination, mental condition has remained much the same. Occasionally, for a few hours at a time, he has been oriented as to place, but never as to time. The defects in memory and the confabulations have been as marked as on entrance. He has talked less and has become more inaccessible. Has failed to recognize his wife and children. He has become more and more careless in habits; does not like to keep his clothes on; lies about exposing his person; soils. Is drowsy a good deal of the time. When walking, carries about with him carefully the corner of his bathrobe, which he smooths out and studies intently. Says it is a blueprint. Is quite contented and more or less happy.

Physical Examination. Patient is a well-developed, well nourished, middle-aged man, of large frame. Inspection shows little except that the face is flushed, while the skin of the rest of the body is a somewhat pasty color. Very slight edema over the feet and lower shins. External examination of eyes and ears negative. Neck negative. Respiratory system negative. Circulatory system negative, except that all heart sounds are distant, but clear. No murmurs. Pulse rate of good quality. Blood pressure 150. Digestive system negative, except that breath is foul; edges of the tongue appear frayed as though bitten. The lesion is old. Tongue is a deep red and there is a deep fissure down the middle. Genito-urinary system negative.

Neurological Examination. Eyes,*—pupils are central; right somewhat larger than the left; both somewhat irregular; react to direct and consensual light stimulation sluggishly and only within narrow limits; react to accommodation. Extra-ocular movements are well performed. No ptosis, nystagmus, nor strabismus. Sensations,— light touch is felt throughout; localizes well. Distinguishes easily the point from head of a pin. No areas of anesthesia or hyperesthesia. Sense of motion and position good. Gait and station normal. No pain on palpation over the deep nerve trunks. Reflexes, biceps and triceps, radials and ulnar jerks present, equal on the two sides. Umbilical and cremasteric reflexes not obtained. Knee jerks very prompt and equal on the two sides. No Babinski, Gordon, or Oppenheim, no ankle clonus. Considerable tremor of fingers on extension, and tremor of fingers in finger to nose test, with some inaccuracy.

Since this examination, patient has grown weaker; gait and station have become more unsteady. Eye signs have remained the same. Tendon reflexes have become diminished.

Laboratory Studies. X-ray examination of the head negative. Examination of the fundi on two different occasions negative.

Blood Examination. Hemoglobin 80%; white count 8200; red count 4,720,000.

Differential: Neut. 50%; lymph. 31%; transit. 18%, eosin. 1%.

Wassermann reaction on the blood negative (several examinations). Wassermann reaction on the spinal fluid negative (two examinations).

	First Examination.	Second Examination.
Cells in spinal fluid.....	2 cells	2 cells
Alb. in spinal fluid.....	N.	+
Glob. in spinal fluid.....	0	0

Colloidal gold test on spinal fluid, negative for syphilis.

Urine Examinations. On admission, nothing noteworthy except a low specific gravity. A series of examinations showed, however, a specific gravity ranging from 1009 to 1036, but usually low. The amount has ranged around 1700 c.c. for 24 hours. Reaction always acid—no sugar. Albumen, usually slight trace. Sediment, occasionally leucocytes and squamous cells, and a few hyaline casts.

Renal function tests were performed on two occasions; the first showed a return of 18%—the second 15%.

1. Total nitrogen in 24-hr. urine specimen 9.47 gms.
2. Total nitrogen in 24-hr. urine specimen 634. gms.
   Urea ..... 5.74 gms.

Chemical Examination of the Blood:

May 13	Total uric acid....	4.37 mg. per 100 gms.	
May 29	" uric acid....	4.0	" " " "
June 17	" non-proteid N.	79.6	" " " "
	" urea	28.	" " " "
June 25	" non-proteid N.	56.5	" " " "
	" urea	28.6	" " " "
	" uric acid.....	4.0	" " " "

* Examination by courtesy of Dr. Holbrook Lowell.

Chemical Examination of Spinal Fluid:

May 19	Total non-proteid N.	30.1	mg. per 100 c.c.
	" urea	23.5	" " " "
May 27	" non-proteid N.	40.	" " " "
	" urea	23.5	" " " "
June 22	" non-proteid N.	28.4	" " " "
	" urea	15.7	" " " "

Study of Hydrogen Ion Concentration:

July 14	24-hr. specimen (not receiving alkali)	6.4
July 15	4.30 A.M., single specimen (not receiving alkali)	5.0
	5.00 A.M., 4 grams bicarbonate of soda administered	
	6.00 A.M., specimen	4.9
	7.00 A.M., specimen	5.9
July 17	10 grains soda bicarb. every hour for 7 hrs. beginning at 6.00 A.M.	
	3.35 P.M., specimen	5.0
	4.00 P.M., specimen	5.2
July 18	25 grains soda bicarb. 6.00 A.M., 12 M., 6.00 P.M.	
	2.00 P.M., specimen	7.5
	5.00 P.M., specimen	8.7
July 19	Alkali same.	
	3.00 P.M.	7.4
	5.00 P.M.	6.7
	11.00 P.M.	6.7
July 20	Alkali same.	
	9.00 A.M.	8.0
	9.00 P.M.	8.6
July 21	Alkali same.	
	9.00 A.M.	6.9
	4.00 P.M.	6.7
	9.00 P.M.	7.8
July 22	Alkali same.	
	9.00 A.M.	7.4
July 23	25 grains soda bicarb. at 6.00 A.M. and 11 A.M.	
	9.00 A.M.	5.9
	5.00 P.M.	7.4

These figures are of interest in view of the recent work of Folin and Denis[11] on the uric acid, urea, and non-proteid nitrogen content of human blood, and the work of Henderson and Palmer on the hydrogen ion concentration in urine,[12] and the presence of an acidosis in cases of nephritis.[13] Folin and Denis obtained results which led them to believe that "from 1 to 2 milligrams of uric acid per 100 grams of blood" to be within the normal variations, although, as they state, these figures may not represent "the full variations." The amount of urea in normal human blood varied, in their studies, from 11 to 13 milligrams per 100 grams blood, the total non-proteid nitrogen from 22-26 milligrams per 100 grams blood.

Mestrezat[14] considers the physiologic limit of urea in the spinal fluid to be 1 gram, or less, per 100 c.c.; the presence of 2 or more grams to be indicative of a "uremic" condition of considerable severity; the prognosis in the presence of 3 grams to be grave. He quotes the work of Widal and Froin,[15] who found in the spinal fluid of "uremic" patients amounts of urea varying from 3.73 to 4.48 grams. In two of these cases no increase of urea was demonstrated in the blood.

In a study of urine acidity, Henderson and Palmer[12] concluded that "normal urine seems to range from a concentration of ionized hydrogen of about 4.82 to one of about 7.45," with an average of 6.03. In a further study[13] upon the effect on the urine acidity of the administration of alkali, they found that the administration of 4 grams of the bicarbonate of soda produced in the normal individual a marked reduction of the acidity in an hour, with the maximum effect in a little over an hour; that the average degree of alkalinity reached after the intake of alkali was 7.60, the average change 1.67. They further concluded that a "condition of acidosis may be assumed to exist when the administration of a quantity of alkali equivalent to one litre of tenth normal solution fails to produce a diminution in the acidity of the urine."

In summary, then, we have on the negative side: (1) no signs of a current infection; (2) no signs indicating increased intra-cranial pressure, as by a tumor; (3) no localizing signs indicative of a cerebral arteriosclerosis; (4) all tests for syphilis negative; (5) spinal fluid findings negative for general paresis or cerebrospinal syphilis.

On the positive side: (1) urinary findings usually associated with chronic interstitial nephritis; (2) apparently poorly functioning kidneys; (3) a retention of nitrogenous products; (4) the presence of an increased amount of nonproteid nitrogen and urea in the blood; (5) an increased amount of non-proteid nitrogen and urea in the spinal fluid; (6) a lack of response to administered alkali, such as is said to be present in an acidosis.

The only fair conclusion that can be made at this time in these cases is that physically they present certain cardiorenal or renal conditions; that mentally, though they closely simulate respectively, catatonic dementia precox, general paresis, or Korsakoff's psychosis, they remain as yet unclassified; but, though they remain without a definite mental diagnosis, a different prognosis and a vastly different treatment is indicated.

In at least one case the patient was saved the stigma of an alcoholic or syphilitic diagnosis

(Chemical studies in the first case from the Peter Bent Brigham Hospital laboratory, Dr. Sallie; chemical studies in the second case by Benjamin H. Ragle, Hilmar O. Koefod, William A. Manuel,—Psychopathic Hospital laboratory.)

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XI.

THE MARGIN OF ERROR IN PSYCHOPATHIC HOSPITAL DIAGNOSES.*

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THE margin of error in the diagnosis of mental disease is a matter of social importance. For upon the medical diagnosis of mental disease hangs the legal decision as to insanity. It is notoriously unsafe to say that a man is insane unless the particular form of mental disease producing his insanity can be specified. To be sure, we often hear that such a man is insane,—but "what kind of insanity" cannot be specified. It is a question, however, whether there are any "kinds" of insanity, at least any kinds corresponding to the forms of mental disease. A man is insane, or he is not insane, or, if there be the so-called demi-insane, the new group either represents an eventual improvement in legal definitions (*e.g.* of grades of responsibility) or else the term demi-insane represents an impossible endeavor to break up the legal term "insanity" into the medical subdivisions of mental disease. Although strictly speaking, the medical man has no more than the ordinary citizen's right to assert insanity, yet practically speaking, the medical man (or as a rule, two medical men speaking as one) has much to say, since his medical diagnosis "mental disease" *may* mean the legal decision "insanity."

If then there are mental diseases from the medical standpoint which are not equivalent to the legal status of insanity, it is clear that the diagnosis of the form of mental disease may rise into a social function of the greatest delicacy. Studies of the error of diagnosis as to form of mental disease should accordingly be made from time to time in properly managed clinics and particularly in those which have the advantage of dealing with numbers of psychopaths (*i.e.* victims of mental disease) that are determined to be not insane.

We accordingly make no apology for the present orientation study of the problems of medical diagnosis at the Psychopathic Hospital, Boston, since it would be difficult to find a clinic more representative of the entire range of psychiatric problems and since a major function of the institution (with its intake running close to 2000 patients a year) is the diagnostic function. Moreover, the time-relations are such, particularly under the provisions of the Massachusetts seven days' "temporary care" law, that rapid diagnosis is a desideratum. Where rapid diagnosis is not merely the usual godsend to the patient, but becomes an official necessity, conditions are particularly favorable to the study of our present day powers in the field of psychiatric diagnosis.

Distributing patients as the Psychopathic Hospital does (under conditions prescribed by the State Board of Insanity), to a number of state institutions, each with its own well-defined traditions in diagnosis, the Psychopathic Hospital has the advantage of having its work controlled by a number of minds.

We should not, however, leave the impression that what we are studying is the accuracy of "snap" diagnoses. The average stay of patients at the Psychopathic Hospital is between two and three weeks, and legal devices are such that in most instances difficult cases can be kept indefinitely for diagnostic or therapeutic purposes. Hence the diagnoses recorded at the hospital are as a rule not snap diagnoses. They are diagnoses made as rapidly as diagnostic devices will permit, under standards intended to be as high as those of the best general and insane hospitals.

Readers who do not know their Massachusetts might believe that the state institutions to which our patients are sent would accede too readily to Psychopathic Hospital diagnoses and hence tend artificially to lower our percentage of error. Those who know the individualistic and fighting spirit of Massachusetts will not fear this diagnostic artifact.

Our point of view in this study is, therefore, to scrutinize the diagnostic results of the Psychopathic Hospital, determine the preventable errors in diagnosis, delimit the region of

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greatest error, and discover the region in which research should best proceed.

Studies of somewhat similar scope had been carried out with Danvers State Hospital material, utilizing, however, autopsied cases and the staff-meeting diagnosis as the basis of analysis.

In 1910 it was shown that, *without* the use of the Wassermann reaction, the accuracy in diagnosis of general paresis might be variously stated as from 85% to 90%.

Orton has published a similar study from Worcester, and Dr. Myrtelle M. Canavan has given us similar figures from the Boston State Hospital. These are embodied in the following table:

TABLE SHOWING ERRORS IN DIAGNOSIS OF GENERAL PARESIS WHERE THE WASSERMANN REACTION WAS NOT EMPLOYED.

	Clinical Diagnoses, Paresis.	Histological Not Paresis.	Diagnoses Not Any Form of Neurosyphilis.
Southard, 1910...	41	6	3
Orton, 1913.....	60	9	8
Canavan, 1914 ...	18	3	2
	119	18	13

Thus general paresis was wrongly ascribed to 18 cases in 119, or in 15%. Neurosyphilis (*i.e.* not merely general paresis, but also other neurosyphilis) was wrongly ascribed to 13 cases in 119, or 11%.

	Clinically Not Paresis.	Proved Paresis.
Southard, 1910.....	186	2
Orton, 1913.....	116	1
Canavan, 1914.....	106	1
	408	4

General paresis has already turned up in 4 cases in 408 cases in which the diagnosis of paresis was never even remotely entertained. A more intensive examination of a number of these 408 would probably somewhat increase this percentage of error.

In 1910, also, another Danvers study was published showing a surprisingly low percentage (66%) of accuracy in the diagnosis of senile dementia, counting as correct such diagnosis in cases having either brain atrophy or coarse brain lesions due to arteriosclerosis. The effect of this study was to point out the existence and numerical importance of senile psychoses which were consistent with normality of brain or with merely microscopic or chemical changes not resulting in visible destruction of brain tissue.

From a third Danvers study of 1910 may be reproduced three tables illustrating the general accuracy of state hospital diagnoses.

TABLE I.

	Cases
Cases at daily clinics, 1904-8, later autopsied....	250
Clinical diagnoses unanimous.....	184
Revised on autopsy data.....	21
Opinions divided or doubtful.....	66
Every opinion incorrect as shown by autopsy.....	7.
Remain as yet obscure.....	10

DIAGNOSTIC ACCURACY.

	Cases
89% with all agreed.....	184
74% some one correct.....	66
85% some or all correct.....	250

TABLE II.

	Cases
Unanimous diagnoses	184
General paresis, clinically.....	42
General paresis, anatomically.....	36
General paresis, errors.....	6
Organic and senile dementia, clinically.....	80
Brain atrophy or cortical arteriosclerosis.....	62
Tumor, lues, porencephaly, *general paresis*.....	4
Total organic, anatomically.....	66
Errors—senile acute psychoses.....	14
Total errors, general paresis.....6+1=	7
Total errors, senile psychoses.....	14

TABLE III.

Doubtful or obscure cases.....		66
One or more diagnosticians right.....		49
Organic and senile dementia	19	
Acute psychoses.....	14	
General paresis.....	9	
Brain tumor.....	4	
Miscellaneous	3	
No diagnostician right.....		7
(One case of each general paresis, cortical arteriosclerosis, organic dementia, streptococcus septicemia, epilepsy, streptococcus meningitis, cerebellar abscess.)		
Obscure, both clinically and anatomically.....		10
Acute psychoses (?).....	6	
Alcoholic insanities (?).....	2	
Deliria (?).....	2	

Similar studies from other state institutions are, so far as we are aware, not available, nor is the present study as accurately controlled as these Danvers and Worcester studies, since we here supplant the autopsy diagnoses with clinical diagnoses. It is upon the background of such a study as this, however, that future controls by extensive autopsy studies can be most effectively made.

In many cases the Psychopathic Hospital officers failed to make a diagnosis, terming the case "unclassified," meaning thereby "psychopathic" in some sense, as a rule also "insane" in the sense of certifiable, but as not capable of further specification. That the officers of the Psychopathic Hospital should not be unwilling thus to confess ignorance was all the more likely on account of the fact that three of its officers (the writers and the chief-of-staff, Dr. H. M. Adler) had been trained at Danvers Hospital, where the habit of leaving cases "unclassified" had become ingrained. The following table shows this:—

UNDIAGNOSTICATED COMMITMENTS.

	In Massachusetts Hospitals.	In Danvers Hospital.	
1904.....	91	26	(29%)
1905.....	93	34	(37%)
1906.....	58	28	(48%)
1907.....	81	18	(22%)
1908.....	92	39	(42%)
1909.....	93	30	(32%)
1910.....	102	44	(43%)
1911.....	119	50	(42%)
1912.....	137	34	(24%)
1913.....	247	41	(16%)
	703	204	(29%)

That this habit of confessing ignorance has been maintained can be seen from tables published in 1913 report of the Psychopathic Hospital, where are given the following figures:—

TEMPORARY CARE GROUP.

Cases	1022	
Unclassified	247	(24 per cent.)
Males	522	
Unclassified	110	(21 per cent.)
Females 500		
Unclassified	137	(27 per cent.)

Analysis shows that the sex-difference is due to the easy resolution of the many more alcoholic and paretic cases among the males which far more than offsets the larger number of "not insane" women in the temporary care group.

VOLUNTARY GROUP.

Cases	362	
Unclassified	68	(19 per cent.)
Males	186	
Unclassified	32	(17 per cent.)
Females	176	
Unclassified	36	(20 per cent.)

Analysis of the voluntary group shows a similar state of affairs to that in the temporary care group. If we combine these figures we arrive at 315 cases unclassified among 1382 diagnoses, *i.e.* 23%.

Of these "unclassified" mental cases, some are to be later resolved through the development of the disease or the accession of new facts, some will remain unresolved through passing prematurely out of observation, some were actually diagnosticable on available facts, and some are essentially not classifiable in the present stage of psychiatry.

We have studied the fate of a group of "unclassified" cases of 1912-1913 as transferred to the institutions receiving the largest number of our cases.

UNCLASSIFIED CASES AMONG THOSE SENT FROM PSYCHOPATHIC HOSPITAL TO VARIOUS INSTITUTIONS, 1912-1913.

	All Cases Sent.	Unclassified.	Remained Unclassified.	Added Unclassified.	Total Remaining Unclassified.
Boston	305	30	3	13	16
Westboro ..	136	40	2	5	7
Taunton ...	91	20	6	2	8
Worcester .	72	23	2	0	2
Danvers ...	29	7	2	3	5
	633	120	15	23	38

It is somewhat curious that the residuum (38 cases) remaining "unclassified" after review by two hospitals should represent 6% of the total. It may be remembered that the Danvers cases of "obscure" mental and anatomical diagnosis (later worked up by L. B. Alford) were 10 in number, representing 4% of the total of autopsied cases then reviewed.

The percentage of cases sent unclassified from the Psychopathic Hospital was in this group 19%, somewhat less than the 23% stated above for the official tables for 1913. The two case-groups are not identical, though they overlap.

Let us now approach the special problems of change of diagnosis in the separate institutions; we will dismiss the "unclassified" group (except for incidental mention) and study the differences of opinion which are definite and presumably based upon differences in observation or interpretation (omitting merely nomenclatural differences so far as possible.)

	Cases All Sent.	Altered Diagnosis.	%	Cases Minus Unclassified.	Altered Diagnosis.	%
Boston	305	89	29	275	62	23
Westboro	136	62	46	98	24	24
Taunton	91	34	37	85	28	33
Worcester	72	31	43	53	12	23
Danvers	29	14	45	22	5	23
	633	2300	36	533	131	25

That is to say, omitting the 19 and 23 cases out of every hundred in which the Psychopathic Hospital fails to make a diagnosis and considering only those in which a definite diagnosis is made, we find that in 25 of every such 100 a change in diagnosis is made.

The later diagnoses have every chance of being more nearly correct than the earlier, but possibly they should not stand so much chance of being better, as these figures might indicate.

Special analyses for the above five institutions may be made as follows:—

The group of cases sent from the Psychopathic Hospital to the main wards of the Boston State Hospital is an important group by virtue of its size and frequent opportunities of interchange of views by members of the Psychopathic and main staffs.

There is a superficial discrepancy of opinion as to 89 in 305 cases (1913), *i.e.* 29%. In 27 of these 89 cases the psychopathic staff was unable to render an opinion other than "unclassified," by which term some form of insanity is meant. These are failures to diagnose rather than errors, so that true discrepancy of opinion is found in 62 cases in 278 where both staffs arrived at some conclusion, that is, in 22%. In 7 cases one of two Psychopathic Hospital diagnoses was pitched on as correct, so that absolute error cannot be laid at the door of the Psychopathic Hospital. This leaves 55 cases to be considered.

A striking feature of this remainder is that the Psychopathic Hospital diagnosis of manic-

depressive insanity is practically never changed (there was one instance, 11589, regarded as infective-exhaustive rather than manic-depressive at the main hospital. The case was one of mania in the course of a pneumonia, and perhaps should be called a symptomatic psychosis, pneumonic type).

On the other hand, the Psychopathic Hospital diagnosis of dementia precox was altered by the main hospital to manic-depressive insanity in some 16 instances. Here possibly there is evidence of two different points of view.

One hundred and thirty-six cases were transferred from the Psychopathic Hospital to the Westborough State Hospital in 1913. In 62 of these (46%) a change of diagnosis was made, but in 38 of these, the change was merely from "unclassified" to a definite diagnosis. Actual differences, therefore, were registered in 24 out of 98 cases (24). But, as in 5 of these the diagnosis became again "unclassified" we are left with 19 cases in which definite diagnoses were rendered by both staffs and disagreement ensued (20%).

Among these 19 cases of disagreement there were five which are of special interest, being alterations from manic-depressive insanity to dementia precox (v. below). There was but one case of the converse change—from dementia precox to manic-depressive insanity (10974)—a fact rather surprising at first blush when the changes of diagnosis at Boston Hospital are considered. Dementia precox was altered to hysteria (10736,—10810), to alcoholic (10938), to imbecile (10972), and to not-insane (10720). Besides the five alterations from manic-depressive insanity to dementia precox, there were four other alterations in the same direction (10625 from general paresis, 10930 from alcoholic, 10,950 from senile dementia [new facts!], 11033 from imbecility). In this connection it is interesting to note that 13 unclassified cases had diagnoses altered to dementia precox, as against 7 unclassified to manic-depressive insanity. Two cases of supposed alcoholic insanity were determined to be manic-depressive (10800, 10824); 10835 became from senile dementia a case of Korsakoff's psychosis; 10893 was altered from organic to senile dementia.

Of 91 cases transferred to Taunton State Hospital, 34 yielded alterations in diagnosis (37%). But 6 of these were from "unclassified," so that the more definite error may be set at 28 in 85 cases (38%). There are four instances in the Taunton review of alterations of our diagnosis of manic-depressive psychosis to dementia precox.

Seventy-two cases were transferred from the Psychopathic Hospital to the Worcester State Hospital in 1913. In 31 of these (or 43%), a change of diagnosis was made, but in 19 of these the change was merely from "unclassified" to a definite diagnosis. Actual differences of opinion, therefore, were registered in 12 out of 53 cases (or 23%). There were no instances in this Worcester Hospital group of alterations from a definite diagnosis to "unclassified."

There were some alterations from one organic group to another, as 28451 (general paresis to tabes and tuberculosis), 28456 (senile to organic dementia), 28395 and 28491 (organic to senile dementia). Two were from dementia precox to imbecility (28150, 28227).

The small group sent to the Danvers Hospital shows a superficial discrepancy of opinion in 14 of 29 cases, or 45%. But, as in the case of Westborough diagnosis, a larger part of the discrepancy comes from the "unclassified" group. There were but 22 cases in which the Psychopathic Hospital risked a diagnosis, and there was a change of diagnosis in 5 of these (23%).

From the above analysis it is easy to conclude that the most difficult field in classification is that of dementia precox. It is not, as might be supposed, that the Psychopathic Hospital officers have a bias in one direction. At first we thought that there was a bias. For we found that the Boston Hospital officers had altered our diagnosis of dementia precox in 16 instances, as stated above; and upon review of the cases we saw good ground for the change in at least 11 of these cases. And, when we found that our diagnosis of manic-depressive psychosis had been altered but once (and then in a case in which the two diagnoses might conceivably be identical), we felt that the Psychopathic Hospital had a true bias against the, as a rule, more optimistic diagnosis of manic-depressive psychosis.

Upon continuing our reviews, however, we found at Westborough that but one case of such an alteration was met with, but that there were 5 instances of alteration of our diagnosis of manic-depressive psychosis to that of dementia precox. At Westborough, too, we found four other cases altered from various diagnoses to dementia precox.

Among the 131 alterations of diagnosis we find the largest single group of alterations to concern the diagnosis of dementia precox or manic-depressive psychosis (42 cases, or 32%). Thirty-five of these cases show a shift of diagnosis from one to the other of these two diagnoses, viz., 20 from dementia precox to manic-depressive and 15 in the reverse direction. Boston yielded four-fifths of the former alteration, and the latter was about evenly divided between Westborough, Taunton and Worcester.

Upon review we consider doubtful or (for external reasons) no longer determinable the issue in 14 cases, leaving 20 which we have more intensively reviewed. In these 20 cases we are inclined to concede the state hospital diagnoses at present.

Eleven of these 20 cases seem to have been excited cases, or cases in which agitation was a feature. We are inclined to believe that the diagnosis of agitated cases is more difficult than that of akinetic cases. It is proposed to throw this problem open in forthcoming diagnostic studies at the Psychopathic Hospital.

Appended are a few condensed histories which struck us as of particular interest.

Three of the five Westborough cases of alteration of Psychopathic Hospital diagnosis of manic-depressive to dementia precox were examples of over-hasty diagnosis at the Psychopathic Hospital. One (10793) should probably not have been diagnosticated at all, as to form of insanity. Another (10634) was partly a language difficulty. A third (10657) illustrates what is so frequently illustrated—the importance of close observation as to hallucinosis.

These three cases may be briefly summarized as follows:—

J. P., Westborough, 10,793 (Psychopathic Hospital 1421) should be placed among unclassified. The case was observed for four days at Psychopathic Hospital, and three days at Westborough before deportation. The diagnosis of the form of insanity must still remain doubtful, although a form of paranoid dementia precox may be suspected. The Psychopathic Hospital diagnosis of manic-depressive insanity was based upon euphoric loquacity, possible flight of ideas, busy interference with all affairs, distractibility. The history secured by Westborough, however, suggests the beginning of a paranoid dementia precox.

A second case might also better have remained unclassified.

S. B., Westborough 10,634 (Psychopathic Hospital 1471), was an illiterate Sicilian, 27 years old, off work six months, said to have been jilted, apathetic, apparently depressed, was thought to show (manic-depressive) retardation during his seven day's observation at Psychopathic Hospital. The *"retardation"* was suspected at the time to be due to difficulties with the interpreter, who did not understand the Sicilian dialect fully. The *apathy* might of course have been that of hebephrenic dementia precox.

In the absence of schizophrenic symptoms, the diagnosis dementia precox has not been favored at the Psychopathic Hospital. It would have been better probably to have left the case unclassified. At Westborough descriptions were obtained of scenic, dreamlike hallucinations (combined visual and auditory), ideas of reference, delusions involving love affairs and religion, as well as a history of previous spells of excitement. It is still difficult to obtain indubitable evidence of schizophrenia (partly dialect difficulty). To sum up, a Psychopathic Hospital error of diagnosis due to erroneous diagnosis of retardation and lack of ability to get history of hallucinations.

The question of the form of diagnosis must take into account hallucinations of God talking "ever since he (patient) was born," telling him always to "walk straight and harm nobody"; and visions of a church burning up with God on the altar, and the Virgin behind God, and of the Virgin unable to fly to heaven although she wished to; or again of a church, with priest saying mass, and his sister playing the organ and angering him, saying, "Why don't you buy a new suit?"

Possibly this case belongs in Kraepelin's dementia paranoides gravis (1913). The lesson appears to be that hallucinosis is the key-symptom for study, and that apparent manic-depressive features should not be urged as basis for a definite diagnosis.

J. H., Westborough, 10,657 (Psychopathic Hospital 1085), was a case in which seven days' observation at Psychopathic Hospital was not enough to establish hallucinosis or interpret a certain amount of resistivism, as well as refusal to eat. Resistivism, mutism, negativism, verbigeration, constrained postures, hallucinosis, delusions of being killed or burned, developed at Westborough within three months. At times tube-fed, at other times patient could be got to eat when told not to eat. After seven months mutism became fixed, and has remained so till present writing.

Two further cases may possibly be examples of two of Kraepelin's newer groups, viz., simple depressive deterioration (11062) and the circular excited form (10988). These cases may be abstracted as follows:—

L. B., Westborough 11,062 (Psychopathic Hospital 2100), gave a history of long, gradual onset (four years from Oct. 29) with worry and crying spells over distasteful work, and with some sex-coloring, perhaps a history somewhat more consistent with the diagnosis dementia precox than with that of manic-depressive insanity. Then came ideas of reference, "must be married tomorrow" to a certain man, "heart down in abdomen," etc. There was an appearance of apathy which the Psychopathic Hospital officers thought might be unreal. At Westborough impulsive acts, persistent covering up with bed-clothes, persistent closure of eyes, silly smiling, and persistence of delusion about heart with exhibition of further sexual-religious delusions (married by Jesus to a Portuguese by proxy; identification of female patients as boys whom she had borne in some unusual way).

This case has much in common with Kraepelin's new simple depressive (or stuporous) deterioration, a form of dementia precox. The case has not been stuporous and has the insidious onset of the non-stuporous form of simple depressive deterioration, as described by Kraepelin. But characteristic terminal mental impairment has not yet set in (8 months after the acute outbreak). The case shows the prodromal character change of (four) years' duration described by Kraepelin. Hypochondria, auditory hallucinations, delusions of persecution, crying spells, sexual excitement, general conduct disorder, are also characteristic. Negativism has now developed, but there is not, as yet, any stuporous tendency like what Kraepelin states to occur in about one-third of cases in this subgroup.

M. H., Westborough 10,988 (Psychopathic Hospital 1873) is a case in which the Psychopathic Hospital diagnosis, after seven days' observations, rested on loquacity, playfulness and general appear-

ance, although there was at times an appearance of listening to voices, and there were occasional statements about being called names. Patient wove relevant remarks into talk, but would not make relevant replies to questions. An idea that "dope," looking and tasting like plaster, is falling from ceiling and walls, might have suggested a paranoid form of dementia precox.

After seven and a half months at Westborough, patient was allowed to leave hospital on furlough with husband. Patient exhibited resistivism, negativism (fell limp on being told to hold stiff), apparently unmotivated laughter and smiling, acts of moderate violence (question of motive), spells of excitement speedily quieted by warm, wet packs (often asked to be kept in pack), hallucinosis (two months after transfer) apparently persistent for four months.

It is possible that this case belongs in the circular excited group of Kraepelin's edition, 1913. The onset was with delusions of persecution, probably on a basis of auditory hallucinosis. Patient was first medically observed in the excited phase which warrants her inclusion in the new group. Distractibility and assimilation of adjacent talk and happenings form a feature suggestive of manic-depressive mania; but these are combined with negativism, impulsive acts, and aimless shifting of attention so as to suggest dementia precox.

Kraepelin states that more than one-half of these cases (53%) have remissions, but these as a rule appear after the initial depression, not as in this case, after a fairly long excited phase. The total course (exclusive of remissions) is rarely as long as two years. The question of diagnosis will probably be resolved shortly.

At this point it is well to consider the single case in which a Psychopathic Hospital diagnosis of dementia precox was altered by Westborough to manic-depressive insanity.

J. B., Westborough 10,974 (Psychopathic Hospital 1858). This diagnosis of dementia precox was erroneous because the remnants of alcoholic hallucinosis (or of delirium tremens, it is not certain which), superimposed on what was probably a manic-depressive excitement gave the impression of dementia precox, especially as conversation, at first relevant, would tail off into irrelevance and incoherence, which taken by itself gave at times a little of the impression of schizophrenia. A history of chancre complicated the picture. In the second month at Westborough patient had an excited attack or exacerbation of excitement *without* hallucinosis and in four more months was about ready to go home recovered. The error might not have been made, had the extent of the patient's previous alcoholism been known (he afterward told of a still previous touch of delirium tremens), and had the picking of imaginary particles from his arms and hands, shortly after entrance, been given due attention.

Six Worcester cases touch dementia precox problems. Three deserve especial study as being alterations from manic-depressive insanity to dementia precox, thus comparable to five instances in the Westborough Hospital group.

L. J., Worcester Hospital 28,191 (Psychopathic Hospital 386), was at Psychopathic Hospital (1) Oct. 19-Nov. 27; (2) Dec. 3-Feb. 6 (becoming a voluntary patient Dec. 7; (3) Feb. 16-17 (Boston police case) receiving both times the diagnosis of maniacal manic-depressive insanity. A period of mutism at first, and in the last residence grimacing incontinence during the prodromal period, persistent and assumption of grotesque attitudes, might have given rise to the suspicion of dementia precox. The serum was positive to the Wassermann test at first, later negative; there seems to have been no clinical evidence of syphilis. Patient, while at Worcester, once gave an account of what were possibly auditory hallucinations of a religious coloring, which, she said, came through a ventilator at the Psychopathic Hospital. Patient was committed to Worcester Feb. 17. In March patient had periods of confusion in the midst of continuous excitement, and had numerous superficial abscesses. Comparative quietude and insight until July, when excited. Another excited spell in August (untidy). Apparent blunting (facial expression) and lack of insight. Scattered thinking. Discharged on trial visit Sept. 24, 1913, "improved." March 27, 1914, mother regarded her as well.

A. B., Worcester Hospital 28,963, has mother who has had several depressions, twice in Westborough Hospital. Patient had four attacks of excitement of about three months each between 18 and 35; as well as numerous depressions, not well remembered, and a tendency to hyperreligiosity. At 43 came the fifth attack of excitement (Psychopathic Hospital), in which the most suggestive symptom which might be regarded as one of dementia precox was drinking sputum from another patient's cup. At onset he cut up his clothes with a razor, walked about naked at a friend's house, and did other similarly odd things. Upon commitment to Worcester, stated that he had no passage in his bowels, later that he was a dead man, and expressed various delusions. The Worcester staff thought at first that the case was manic-depressive (possibly dementia precox) but in the course of five months altered the diagnosis to dementia precox. There seems to be no evidence of hallucinosis at any time, or of characteristic catatonia. The delusions remind one of involution-melancholia.

XII.

On the Systematic Control of Salvarsan Therapy Based on the Rapidity of Arsenic Excretion.*

By H. M. Adler, M.D., Boston,

Chief-of-Staff, Psychopathic Hospital, Boston; and Assistant Professor of Psychiatry, Harvard Medical School.

Attention has recently been focused upon the treatment of syphilitic diseases of the nervous system, both because a new treatment has been

* Being Contributions from the Psychopathic Hospital, Boston, Number 62 (1914.28), read at the Second Annual Conference on the Medical and Social Work of the Psychopathic Hospital, June 26, 1914. *(Bibliographical Note.*—The previous contribution, Number 61 (1914.27), was by E. E. Southard and A. W. Stearns, entitled "On the Margin of Error in Psychopathic Hospital Diagnoses," published in the Boston Medical and Surgical Journal, Vol. clxxi, No. 24, December 10, 1914.

proposed by Ehrlich for diseases which until recently have seemed outside the reach of older methods, and also, largely because therapy in nervous diseases, and especially in mental diseases is very restricted in amount.

With the introduction of salvarsan therapy, and especially with the general use of intradural injections of salvarsanized serum as proposed by Swift and Ellis, it has seemed a comparatively simple matter to treat syphilis of the nervous system, and the first reports apparently confirmed this idea. It did not take long, however, for some opposition to arise, and unfavorable reports appeared in the literature, which were explained in various ways by different authorities. Thus, Ehrlich explained the failure of salvarsan to cure, even after repeated injection, cases of syphilis of the central nervous system as general paresis, by the consideration that there were within the body certain dead spaces which were not reached by drugs circulating in the blood stream. One of these dead spaces, according to Ehrlich, is the subarachnoid space. And Ehrlich supposes that the spirochaetae that are located here, escape the effect of salvarsan and thus continue to cause local disease, and form the foci for a spread of new infection.

Swift and Ellis, on the other hand, have attacked this so-called dead space by direct injection of salvarsan in such a fashion that its extreme toxic effects do not ensue.

All of the methods employed have been based upon the original statement of Ehrlich that a single large dose of salvarsan could suffice to kill all the spirochaetae that could be reached by the drug, and the only reason for repeated injections in syphilis of the nervous system is the existence of these dead spaces in which the spirochaetae lurked.

It would seem then, that a single injection into the cerebrospinal fluid should effectually kill off all organisms not reached by the blood path. Apparently the results of the Swift-Ellis method are that the syphilitic processes in the ependyma are improved or cured but no effect is had upon those organisms which are within the cerebrospinal axis itself.

It has seemed worth while, however, to determine whether the salvarsan when injected in these ways acted in a specific and rapid fashion, or whether there might not be certain conditions affecting the assimiliation and excretion of the salvarsan, which, while having no bearing upon the specificity of the drug, might yet impair its efficacy.

Several methods for determining arsenic in organic combinations or in the presence of organic substances are known, and all are characterized by apparent simplicity and extreme delicacy. They are so simple that they tempt even the beginner, and they are so delicate that they yield quantitatively astonishing results when applied to material that might be supposed to be arsenic-free. This fact has given rise both to a literature which is remarkable for its discrepancies, as well as to a certain skepticism on the part of the more careful workers toward reports on arsenic findings.

The methods adopted in this investigation were R. L. Emerson's modifications of the Marsh and Gutzeit test. The chemical determinations were carried out by one of us (Arthur Wetmore) in careful training under the personal supervision of R. L. Emerson, Assistant Chief of the Bureau of Chemistry, Washington, D. C.*

The determinations were 153 in number. Of these 15 were performed upon cerebrospinal fluid withdrawn twenty-four hours after the injection of salvarsan intravenously. Fifteen determinations were made upon the blood of patients before they had received salvarsan treatment. One hundred and twenty-three determinations were performed upon the blood of patients at different intervals after injection of salvarsan. The number of patients tested in one way or another was 24. Of these seven cases were examined as controls. The number of cases in which the determinations were made before and after treatment was 17. There were from two to 30 determinations upon each patient.

Two were done without any previous intravenous injection of salvarsan. Ten were done 24 hours after intravenous injection. One was done 48 hours after intravenous injection, and one at 15 days. One had 48 hours after intravenous injection and 24 hours after intraspinous treatment. No As_2O_3 was recovered from any one of these.

The arsenic was found absent in the blood as early as 24 hours after intravenous injection. The majority of cases were found to be arsenic-free in from 36 to 48 hours after salvarsan injection. The longest interval after injection that arsenic was recovered from the blood was 16 days in one case.

In view of the interest existing in the Swift-Ellis method of injecting salvarsanized serum, the following may be noted:

The average amount of As_2O_3 per gm. of blood at end of one hour after .6 gm. of salvarsan=3.248 mmg.

3.248 x 2.07=6.73 mmg. of salvarsan.

6.73 x 12 (cc. of serum injected)=70.76 mmg. salvarsan in 12 cc. of serum. This follows if the salvarsan is equally distributed between serum and formed elements.

* The details of these methods have not yet been published and may be obtained from Dr. R. L. Emerson, Bureau of Chemistry, Washington, D. C.

TABLE I.

Time after Injection of Salvarsan.	Dose of Salvarsan Injected.	No. of Determinations.	Maximum Yield of As_2O_3 expressed in mmg.	Maximum Yield of As_2O_3 expressed in mmg.	Average.
30 seconds	.25	2	33.3 mmg.	7.5 mmg.	20.4 mmg.
"	.3	14	20.8	2.34	10.44
"	.6	8	26.78	8.9	16.82
30 minutes	.3	1			2.08
"	.6	2	9.3	8.33	8.81
1 hour	.3	7	2.85	1.47	2.208
"	.6	2	4.166	2.33	3.248
3 hours	.3	2	0.553	.25	.401
24 "	.3	8	2.5	.0	.398
"	.6	3	.272	.0	.157
30-31 hrs.	.2	7	1.0	.5	.21
"	.3	1			.0
33-36 hrs.	.2	1			.0
"	.3	1	1.0		1.0
"	.5	1			.0
"	.6	2	2.	1.	1.5
45-53 hrs.	.3	4	.083	.0	.0208
"	.6	5			0.
72 hours	.3	6	.214	.0	.035
"	.6	6	.16	.0	.05
4 days	.3	1			.5
"	.6	2	1.5	1.	1.25
5-6 days	.2-.3	5	.625	.0	.0125
"	.5-.6	4			0.
7 days	.25-.3	14	.285	.0	.038
"	.6	8	.5	.0	.101
7+days	.3	6	.174	.0	.029

INTERVAL OF 30 MINUTES.

No.	Name.	Dose.	As_2O_3 in mmg.	
103	W. R.	.6	26.78	
116	"	.6	26.7	
121	"	.6	19.5	
128	"	.6	16.6	
139	"	.6	17.04	
136	C. D.	.3	10.09	girdle sensation
145	"	.3	5.5	
89	M. M.	.3	8.92	
114	"	.3	10.9	
126	"	.3	2.34	
91	J.M.	.3	7.81	
93	M. B.	.25	7.5	
95	J. B.	.25	33.3	
97	L. M.	.3	3.6	
108	"	.6	10.00	
123	"	.3	10.000	
132	"	.6	9.09	
143	"	.6	8.9	
100	F.S.	.3	9.72	
111	"	.3	14.5	
125	"	.3	10.9	
130	"	.3	15.6	Fainted
134	H. F.	.3	15.6	
141	"	.3	20.8	Vomited
117	W. R.	.6	9.3	
109	L.M.	.6	8.33	
112	F. S.	.3	2.08	

INTERVAL OF 1 HOUR.

17	W. R.	.9 n.	4.166	
29	"	.9 n.	2.33	
33	J. R.	.45 n.	2.5	
16	C. D.	.45	2.85	
13	A. D.	.45	1.47	
27	"	.45	1.78	
31	C. D.	.45	2.72	
35	F. H.	.45	2.14	
15	M. C.	.45	2.0	

INTERVAL OF 24 HOURS.

No.	Name.	Dose.	As_2O_3 in mmg.	
38	W. R.	.9 n.	0.272	
71	A. S.	.3 s.	0.000	
37	J. R.	.45 n.	0.222	
36	A. D.	.45 n.	0.0454	
39	C. D.	.45 n.	0.285	
50	F. H.	.45	0.142	
75	J. R.	.6 s.	2.000	Vomited
76	A. C.	.3 s.	2.5	Chills
70	M. M.	.3	0.000	
138	H. F.	.3	0.000	

INTERVAL OF 30-31 HOURS.

54	W. R.	.3	0.000	
55	J. R.	.3	0.000	
56	F. D.	.2	0.000	
63	"	.2	0.5	
57	A. S.	.2	0.000	
62	"	.2	0.000	
58	B. B.	.2	0.000	
61	"	.2	1.000	

INTERVAL OF 33-36 HOURS.

60	W. R.	.5	0.000	
72	"	.6	1.000	Malaise-thrombus
73	J. R.	.6	2.000	Sick
64	C. C.	.2	0.000	
74	"	.3	1.000	Chills

INTERVAL OF 45-51 HOURS.

50	W. R.	.9 n.	0.000	
83	"	.6	0.000	
150	"	.6	0.000	
49	J. R.	.3	0.083	
81	"	.6	0.000	
51	C. D.	.3	0.000	
148	"	.3	0.000	
82	C. C.	.3	0.000	
149	L. N.	.6	0.000	

INTERVAL OF 72 HOURS.

84	W. R.	.6	0.000	
104	"	.6	0.0953	
119	"	.6	0.16	
140	"	.6	0.000	
142	H. F.	.3	0.000	
146	C. D.	.3	0.000	
144	L. M.	.6	0.000	
87	J. M.	.3	0.214	
147	F. S.	.3	0.000	
105	L. M.	.3	0.000	
106	F. S.	.3	0.000	
118	"	.6	0.05	

INTERVAL OF 4 DAYS.

80	W. R.	.6	1.000
78	J. R.	.6	1.5
79	C. C.	.3	0.5

INTERVAL OF 5-6 DAYS.

46	W. R.	.9 n.	0.000
47	J. R.	.45	0.000
65	W. R.	.6 (5 or s.)	0.000
59	J. R.	.5	0.000

No.	Name.	Dose.	As_2O_3 in mmg.	
48	C. D.	.45 n.	0.0625	
67	F. D.	.25 s.	0.000	
66	J. R.	.6	0.000	
68	A. S.	.2	0.000	
69	C. C.	.2	0.000	
		INTERVAL OF 7 DAYS.		
7	W. R.	.9 n.	0.000	
28	"	.9	0.111	
102	"	.6 s.	0.000	
115	"	.6 s.	0.000	
120	"	.6	0.100	
32	J. R.	.45	0.000	
30	C. D.	.45	0.285	
26	A. D.	.45	0.000	
86	A. S.	.3 s.	0.000	
85	M. M.	.3	0.000	
88	"	.3	0.000	
113	"	.3	0.000	
127	"	.3	0.000	
129	W. D.	.6	0.5	
92	M. D.	.25	0.000	
94	J.B.	.25	0.000	
107	L. M.	.6	0.000	
122	"	.6	0.000	
133	"	.3	0.000	
110	F. S.	.3	0.000	
124	"	.3	0.000	
131	"	.3	0.24	Fainted
		INTERVAL OF 7 DAYS.		
52	W. R.	27	.9 n.	0.000
53	J. R.	27	.3 s.	0.000
5	C. D.	16	.9 n.	0.174 Upset
8	"	20	.45	0.000
137	"	63	.3 s.	0.000
90	J. M.	10	.3	0.000

Basing our therapy upon these findings, we determine in cases presented for treatment what the interval is between injection of salvarsan and the disappearance of arsenic from the blood, and repeat the dose of salvarsan at the end of the shortest interval thus determined.

If the blood is arsenic-free 24 to 48 hours after the injection of salvarsan, we have found it convenient to repeat the injection of salvarsan at intervals of three days. In the occasional case in which the arsenic disappears at a slower rate from the blood, this interval must be increased. We have found that salvarsan therapy thus controlled is borne well by the patient, and we have so far not obtained any of the unpleasant symptoms of salvarsan in diseases of the nervous system.

The cases which show the untoward symptoms after inhibition of salvarsan (such as the Herxheimer skin reaction, temperature rise, fainting, epileptic convulsions) are precisely the cases which show a delay in the excretion of the arsenic.

The major portion of the arsenic is excreted the first few hours after injection, and apparently the size of the dose has no effect upon the period of excretion. Increased tolerance to salvarsan seems to run parallel to increased rapidity of excretion.

We add a table showing examinations of cerebrospinal fluid for arsenic at varying intervals after injection of salvarsan intravenously. It is interesting to note that each examination resulted negatively. The significance of this cannot be discussed here beyond the statement that it corroborates Ehrlich's findings and is in accord with his statement to the effect that the sub-arachnoid space cannot be reached by injection of salvarsan into the blood stream.

TABLE.

Date.	No.	Initial.	Interval.	Dose.	Result.
Mar. 15, '14	G.	R. G.	48 hrs.	.0	0
Mar. 15, '14	2	W. R.	48 hrs.	.9 neo.	0
Mar. 16, '14	3	W. R.	24 hrs. intersp.	.10 c.c.	0
Mar. 28, '14	22	W. R.	24 hrs.	.9 neo.	0
Mar. 28, '14	23	W. R.	24 hrs.	.9 neo.	0
Mar. 15, '14	4	C. D.	15 days	.45 neo.	0
Mar. 21, '14	20	C. D.	24 hrs.	.45 neo.	0
Mar. 28, '14	44	C. D.	24 hrs.	.45 neo.	0
Mar. 20, '14	12	A. D.		.0	0
Mar. 21, '14	25	A. D.	24 hrs.	.45 neo.	0
Mar. 28, '14	41	A. D.	24 hrs.	.45 neo.	0
Mar. 21, '14	18	C.	24 hrs.	.45 neo.	0
Mar. 21, '14	24	J. R.	24 hrs.	.45 neo.	0
Mar. 28, '14	42	J. R.	24 hrs.	.45 neo.	0
Mar. 28, '14	45	F. H.	24 hrs.	.45 neo.	0

Book Reviews.

Plain Rules for the Use of Tuberculin. New York: William Wood and Company. London: R. Allan Bennet.

This small book of forty-eight pages, attractively published, will prove of great value to a small group of physicians, chiefly to those in the sanatoria and other institutions, who wish to take up the use of tuberculin in diagnosis and in treatment.

The print is large and clear. There are wide margins and the subject matter is divided into paragraphs and headings. There are ten illustrated charts.

As the author says, "This small book is written simply as a guide to those who are intending to work out for themselves some of the problems of tuberculin treatment." As such, it will be of distinct value.

A Manual of Biological Therapeutics. Detroit, Michigan: Press of Parke, Davis and Company. 1914.

This book presents, from a commercial stand point, the therapeutics of sera, bacterins, phylacogens, tuberculins, glandular extracts, and antitoxins. It is illustrated by a number of full-page plates, many of which are colored.

Stedman's Medical Dictionary. By THOMAS L. STEDMAN, A.M., M.D., Editor of the *Medical Record,* etc. Third edition. Royal 8vo., 1079 pages, illustrated. New York: William Wood and Company. 1914.

A third edition of this dictionary has appeared during a period of three years. The explanation of this success is not difficult to understand when one considers the admirable form in which it is published as well as its succinct and adequate subject matter. In the rapidly changing nomenclature of modern medicine, new terms are continually being added and these it is the function of a lexicographer to appraise, accept or reject. In this laborious work the author has found it necessary to increase the size of the book by thirty pages. As a matter of fact, it was necessary to destroy the old plates and to revise the entire book. We cordially commend this dictionary to physicians and all others who find it necessary to use medical terms.

The Pharmacy Handbook. By F. W. CROSSLEY-HOLLAND, F.C.S. London: Henry Frowde, Hodder and Stoughton. 1914.

This volume in the series of Oxford Medical Publications aims to present, in form convenient for ready reference, "information upon matters which come within the purview of the practising pharmacist." It is not a manual of technical pharmacy, but rather a guide to the art and ethics of drug dispensation. Though particularly adapted to the conditions of pharmaceutical practise in England, its suggestions are equally applicable, *mutatis mutandis,* to the United States. There is an excellent terminal bibliography.

Chemistry for Nurses. By REUBEN OTTENBERG, A.M., M.D. New York: The Macmillan Company. 1914.

This new manual of elementary chemistry is designed to supply to nurses such knowledge of that science as is needful for an intelligent appreciation and application of the principles of materia medica, physiology, and dietetics. The subject has often hitherto been neglected in the instruction in training-schools, yet its importance is obvious, and is evidenced by the appearance of questions in chemistry on examination papers for nurses' registration in 22 states of the Union. The book represents the author's lecture-course to pupil nurses at the Mount Sinai Hospital, New York. It is simple, clear, and straightforward in style, and describes only such fundamental experiments as can readily be performed before a class, or by individuals, with a minimum of equipment. It is a convenient, brief compendium and should prove of definite value in the teaching of nurses.

Diseases of the Bones and Joints. By LEONARD W. ELY, Associate Profesor of Surgery, Leland Stanford, Jr., University, San Francisco, Cal. New York: Surgery Publishing Company.

This book of some two hundred pages by Ely is an important contribution to medical literature. It does not aim to be exhaustive and is in no sense a text-book. Its consideration of certain important subjects is meager and sketchy, if one may use the word. With many isolated statements, moreover, one does not necessarily agree, but one cannot fail to be convinced that the author is expressing views based on personal experience and careful observation, both clinical and microscopic. This certainly is a rare combination. There is a stimulating freshness in the author's point of view, and the style is vigorous, concise, and frequently almost epigrammatic.

The first chapter, on the Anatomy, Physiology, and Pathology of Bones and Joints is admirable, and one reads to the end of the work wishing frequently that the author would expand his views more fully, but never wearied by diffuseness.

The convictions expressed regarding the nature of tuberculous disease of the bones and joints seems to be well supported by pathologic proof. The bearing which they have on operative and conservative therapy is important. The illustrations are many and comprise both photomicrographs and illustrations of methods of treatment. We commend the book highly and trust that it may have a wide reading, not only by orthopedic surgeons, but by the medical profession generally.

Surgical Diseases and Injuries of the Genito-Urinary Organs. By J. W. THOMSON WALKER, M.B., C.M., Ed.; F.R.C.S., Eng.; Hunterian Professor of Surgery and Pathology, Royal College of Surgeons of England (1907); Surgeon to the Hampstead General and North-West London Hospital; Assistant-Surgeon to St. Peter's Hospital for Stone; Urinary Surgeon to the Radium Institute. With 24 colour and 21 black-and-white plates, and 279 illustrations in the text. 8vo. 790 pages. New York: Funk and Wagnalls. 1914.

This book presents its material from the anatomical point of view as to arrangement and its eleven parts, each containing a number of chapters, have the following headings: 1. The Kidney. 2. The Ureter. 3. The Bladder. 4. The Urethra. 5. The Prostate. 6. The Seminal Vesicles and Cowper's Glands. 7. The Testicle. 8. The Tunica Vaginalis. 9. The Spermatic Cord. 10. The Scrotum. 11. The Penis.

In his preface the author explains this point of view as follows: "I decided to retain the anatomical classification for the reason that this work lays no claim to be a purely scientific treatise on the diseases of the genito-urinary organs, but is intended to serve as an aid to clinical work; and my personal experience of using text-books arranged in the anatomical and in the pathological classification is that it is easier to refer to the former in an obscure case, than to the latter."

The subject matter is presented in simple language and contains the knowledge of this large field of surgery brought up to the present moment. The book is essentially a practical book written by a working surgeon, and this fact is constantly manifest even in such portions of the work as so often receive scant attention in books of this kind. The pathology, for instance is presented from the operating-room point of view and not from that of the autopsy room, while the illustrations, x-ray pictures, cystoscopic drawings, etc., are for the most part taken directly from cases and not from other books. The author has shown wisdom as well as wide knowledge in the presentation of his subject, and he has presented existing facts and beliefs of the day with great completeness, at the same time leaving no doubt in the reader's mind of his (the author's) own opinion on any point at issue. This is not only a valuable book, but is a most satisfactory and attractive one, for the orderly mind and pleasant pen of its author present his mature experience, both as a surgeon and as a teacher, in a way which cannot fail to give the contents their greatest value. The index is carefully compiled, and the paper and type are adequate.

The Clinics of J. B. Murphy, M.D., at Mercy Hospital, Chicago. April, June, August. 1914.

These three bi-monthly volumes, in a familiar form, are as interesting as ever. In the April number there are twelve chapters, including one on the Thyroid; one upon Bleeding Hemorrhoids, with a discussion on Anemias by Dr. Charles L. Mix, and one on Duodenal Ulcer. The June number contains fourteen articles. One of these articles is described as being Dr. Murphy's Clinical Talks on Surgical and General Diagnosis: this contains Dr. Murphy's idea of radical operation of cancer of the breast; also an article on surgery of tendons, and a series of bone cases. The August number is a little larger than the others. It includes among its sixteen topics: Arthroplasty of Hip, Facial Paralysis, Spinofacial Nerve Anastomosis, Hysterectomy, Cerebellar Tumor, and Recurrent Luxation of Left Patella. These volumes as usual well repay examination by the operating surgeon.

Physiologie Normale et Pathologique des Reins. Par L. Ambard, Chef du Laboratoire de Chimie de la Clinique des Maladies des Voies Urinaires a l'Hôpital Necker. Paris: F. Gittler. 1914.

Manuel de Cystoscopie. Par E. Papin, Chef de Clinique des Voies Urinaires a l'Hôpital Necker. Preface par M. le Professeur F. Legueu. Paris: F. Gittler. 1914.

Notions Pratiques D'Electrothérapie Appliquée à L'Urologie. Par Le Docteur Denis Courtade, Ancien interne des Hôpitaux, Chef de Laboratoire à la Faculté de Médecine, Membre de la Société de Urologie, Lauréat de l'Institut. Paris: F. Gittler. 1914.

These books, each containing from two hundred to three hundred pages, are three of the five volumes which have recently been published (June, 1914) from the "Clinique des Maladies des Voies Urinaires de Necker."

The first volume deals with various experimental physiological problems connected with normal and pathological kidneys, chiefly from studying their urines. It then classifies the various types of nephritis, discusses their prognosis and their influence upon other body functions, and ends with a valuable chapter containing studies of renal function in surgical cases.

Volume two devotes itself to cystoscopy—its history, technic, armamentarium, and its usefulness in the field of diagnosis. It presents little which is new or individual, although it portrays our knowledge of cystoscopy with completeness; but the detail of its descriptions is so carefully carried out both in the text and in the illustrations as to make the book of real value, especially to the student.

The third book might well be, and probably is, a series of lectures on electro-therapy as applied to genito-urinary diseases. After introductory chapters which consider the various forms of electrical currents and batteries, the main body of the book concerns itself with the usefulness of electricity in the treatment of conditions both functional and organic which involve the genito-urinary organs. The book contains much to interest the urologist, but those whose work is largely developed along the lines of major genito-urinary surgery will be perhaps disinclined to share the author's ideas as to the value of electrical treatment in such conditions, as for example, hypertrophy of the prostate and stricture of the urethra.

All three volumes are properly presented. The type and paper are good and the illustrations are for the most part both excellent and original, and are, as a whole, better than such hospital reports ordinarily contain.

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MEDICAL STATUS OF THE UNITED STATES NAVY.

THE recently published annual report of Dr. W. C. Braisted, Surgeon General of the United States Navy, records the medical status of this service for the fiscal year 1914. During the year 1913 the health of the navy was good and showed a satisfactory improvement over the preceding year. The total sick days in 1913 showed a slight increase over 1912, but the death rate in 1913 was only 3.82 as against 4.08 in 1912. Among the diseases of special interest, comment is made on malaria, diphtheria, small-pox, typhoid fever, tuberculosis, venereal diseases, appendicitis, alcoholism and mental disorders. A slight increase in the incidence of malaria is accounted for by the sojourn of vessels in Mexican waters. Although the admission rate of diphtheria had increased there were no deaths from this disease. The outbreak of small-pox on the Ohio, which was described in contemporary issues of the JOURNAL caused a total of twenty-nine cases and five deaths. The number of typhoid fever was only twenty-two, with four deaths, a total rate of 0.33 per thousand, the lowest annual rate yet recorded in the service. All the cases which occurred were in men who had not received antityphoid inoculation or in whom the inoculation had not been complete. There were 367 cases of tuberculosis during the year. The incidence of all the venereal diseases has shown a steady decrease since 1911, presumably attributable to the required employment of venereal prophylaxis. There were 168 cases of appendicitis with no deaths. Alcoholism is also steadily on the decline in the navy, the incidence rate per thousand in 1913 being only 3.45. There was a slight increase in mental disorders whose rate was 4.11 in 1913 as against 3.97 in 1912. A method is under consideration for more accurate detection of mental defectives on enlistment in the navy with a view to excluding such individuals at the recruiting stations and thereby reducing the cost at the naval prisons and hospitals.

Detailed consideration is given to sanitary measures and conditions afloat, ashore, and in general. The navy ration is discussed, and, though considered excellent in quality and sufficent in quantity, is criticised as excessive in meat and fats, especially for tropical service, where an increase of vegetables and fruits would be desirable. The white uniforms also are criticised as particularly disadvantageous in war, when khaki or forestry green would be preferable, as well as more serviceable at all times for wear aboard ship. First aid instruction has been given to all enlisted men by division officers, but might, it seems, be more satisfactory in the hands of the medical corps. It is suggested that a paymaster should be added to the complement of officers on hospital ships, who should also act as commissary.

A larger number of hospital ships is urgently necessary, at least one for each fleet. A plan is being perfected for the rapid transformation of merchant ships for this purpose.

Special reports are made of sanitary conditions at the Annapolis Naval Academy, at the naval stations at Guam, Guantanamo, and Samoa, at the Philadelphia Navy Yard, and at the various naval hospitals. In general it is felt that an abundance of recreation and liberty is advantageous for the welfare of the enlisted man. Athletic exercises are particularly encouraged. Systematic education of the enlisted personnel of the hospital corps is undertaken, especially in anatomy, physiology, emergency surgery, bandaging, field and personal hygiene and sanitation. A detailed description is given of the activities of the navy medical corps during the United States occupation of Vera Cruz

beginning on April 21, 1914. A field hospital was located in a frame building at one of the piers and the ambulance party so divided as to render effective aid to the different companies. Members of the hospital corps and stretcher bearers were highly commended in orders for efficiency and courage under fire.

During the year ended June 30, 1914, twenty-eight medical officers were admitted to the corps and ten were lost by death, retirement and resignation, leaving the total strength at 311 with 36 vacancies. The services of officers of the medical reserve corps were utilized at recruiting stations and on several ships. There are thirteen vacancies in the navy dental corps, which has proved itself of great value. The hospital corps consist of twenty-four pharmacists, 285 hospital stewards, and 1128 hospital apprentices, a total of 1437. Even this number, however, is inadequate properly to man the hospitals, ships and stations of the service even in times of peace. A hospital corps training school has recently been established at Newport, R. I., to teach newly enlisted apprentices. During the year, 43 nurses have been appointed to the naval nurse corps and 38 have left the corps. At Guam and Samoa gratifying progress has been made in the instruction of native women and nurses.

The medical department of the United States Navy seems, therefore, in a creditable state of efficiency and preparation to meet the demands of a peace footing. Whether it would be able, without greater appropriations, to extend its activities rapidly and adequately in the event of war is a question involved in the entire problem of our general national status of naval efficiency.

THE EPIZOÖTIC OF FOOT AND MOUTH DISEASE.

ON Monday of last week, Nov. 30, certain counties of Wisconsin, Illinois, and Iowa were, by order of the United States Department of Agriculture, freed from some of the restrictions of the federal livestock quarantine for foot and mouth disease.

"All the counties in Wisconsin are released with the exception of Green, Rock, Walworth, Kenosha, Racine, Dane, Jefferson, Waukesha, Milwaukee, Lincoln and Langlade.

"In Iowa all counties are released except Mitchell, Greene, Blackhawk, Buchanan, Delaware, Dubuque, Tama, Benton, Linn, Jones, Jackson, Poweshiek, Iowa, Johnson, Cedar, Clinton, Scott, Keokuk, Washington, Louisa and Muscatine.

"The following counties in Illinois are released: Calhoun, Madison, Bond, Fayette, Effingham, Jasper, Crawford, St. Clair, Clinton, Marion, Clay, Richland, Lawrence, Monroe, Washington, Jefferson, Wayne, Edwards, Wabash, Randolph, Perry, Franklin, Hamilton, White, Jackson, Williamson, Saline, Gallatin, Union, Johnson, Pope, Hardin, Alexander, Pulaski and Massac."

The release order provides that cattle for immediate slaughter may be shipped from these counties in interstate commerce, and that cattle may be received for feeding purposes, but may not be shipped for feeding elsewhere.

Thus far during the course of the epizoötic a total of 1800 infected animals has been slaughtered in Massachusetts,—424 cattle, 1267 fowl, 104 swine, 2 sheep, 2 oxen, and 1 goat. About 600 more infected animals remain to be slaughtered in this state.

On Nov. 30, four new cases of foot and mouth disease among cattle were discovered at Pelham, and one at Amherst, N. H.; and 7 cases at Groton City, near Ithaca, N. Y. On Dec. 1 another case was found at South Warren, and on Dec. 2 others at Swampscott, Mass. More infected cattle were slaughtered at Medford, Mass., on Dec. 2. The cost of the epizoötic thus far to this Commonwealth is now estimated at $150,000.

TWO MORE AMERICAN HOSPITALS IN EUROPE.

IN last week's issue of the JOURNAL we commented editorially on the two American hospitals established respectively at Paris and Munich by Americans resident in those cities. Report from Petrograd and London now announces the opening on Nov. 27 of another American hospital of 50 beds at Warsaw, Poland, in the presence of the governor-general and the consuls of friendly nations. The money for this enterprise was raised in Chicago under direction of the Polish-American Society. On Nov. 28 another American hospital of 40 beds, equipped by Americans resident at Petrograd, was opened in that city with addresses by Mr. Marye, the United States ambassador, by the mayor of Petrograd, and by other Russian offi-

cials. These two new American hospitals in Europe, like those at Munich and at Paris, deserve the cordial and generous financial support of Americans at home, for their work stands not only to the credit of American charity but also to the advancement and honor of American medical science abroad.

MEDICAL NOTES.

OBSERVANCE OF TUBERCULOSIS DAY.—By appointment of the National Association for the Study and Prevention of Tuberculosis, Sunday, November 29, was appropriately observed throughout the United States as Tuberculosis Day.

POLIOMYELITIS IN OCTOBER. — During the month of October, 30 cases of poliomyelitis were reported in Massachusetts, 11 in Virginia, 10 in Wisconsin, and 9 in Mississippi. Of the Massachusetts cases, 5 were in Haverhill and 4 in Boston.

AMERICAN PUBLIC HEALTH ASSOCIATION.—The annual convention of the American Public Health Association was opened at Jacksonville, Fla., on Nov. 30 and continued through Dec. 4. Among the principal speakers were Dr. William C. Woodward, of Washington, D. C., president of the association; Dr. Frederick R. Green, of Chicago; Dr. Charles V. Chapin, of Providence; and Dr. George H. Shaw, of the United States Department of Agriculture. On Dec. 2 a joint session was held with the National Mouth Hygiene Association, at which addresses were made by Dr. Harvey W. Wiley and Mr. Frederick L. Hoffmann. On Dec. 4 Prof. William T. Sedgwick was elected president for the ensuing year. The meeting of 1915 will be held at Rochester, N. Y.

TYPHOID FEVER IN SPAIN.—Report from Paris on Nov. 25 states that a severe epidemic of several thousand cases of typhoid fever is now prevalent at Barcelona, Spain.

EUROPEAN WAR NOTES.—On Dec. 1, the Chicago Red Cross fund amounted to $104,000. The total amount of money thus far raised in that city for European war relief is $427,000.

On Dec. 5, the total of the New York Belgian relief fund amounted to $597,250.90, the New York Red Cross fund to $368,752.91, and the American Ambulance Hospital fund to $184,056.98.

On Dec. 6, the total of the New England Belgian relief fund amounted to $126,670.90, the Massachusetts Red Cross fund to $83,027.43, and the Boston branch of the American Ambulance Hospital fund to $40,549.95.

As a result of the appeal recently made, contributions of money and clothing have been received for the American Hospital at Houlgate, France. Further quantities of medical and surgical supplies are to be forwarded to this institution by steamer sailing on Dec. 12.

BOSTON AND NEW ENGLAND.

AWARD OF JOHN HARVARD FELLOWSHIPS.—The John Harvard Fellowships in the Harvard Medical School for the present year were formally awarded at a meeting in the Administration Building on Wednesday, Dec. 2, at 5 P. M. There was an address by Professor Theobald Smith, after which awards of the fellowships and of honorable mention were made by the Dean, Dr. Edward H. Bradford. Following the presentation of fellowships, an informal reception was held by the Harvard Medical Students' Association.

PREVALENCE OF DIPHTHERIA IN BOSTON.—During the month of November there were 408 cases and 18 deaths of diphtheria in Boston, much larger numbers than in any preceding month this year.

SOCIETY FOR THE PREVENTION OF CRUELTY TO CHILDREN.—The thirty- sixth annual meeting of the Massachusetts Society for the prevention of Cruelty to Children was held Tuesday, December 1, 1914, at the Hotel Vendome, Boston. Mr. C. C. Carstens, Secretary and General Agent of the Society, announced that the Society had investigated 4,848 cases in the last twelve months and had under its protection 12,513 children during the same time,—more than 1,000 children a month. 965 cases were prosecuted in the courts on behalf of 2,636 children. In the Boston office alone, 144 parents were prosecuted for non-support and neglect of their minor children, while 40 people were brought to justice for sex crimes against young girls.

In addition to the central office at 43 Mt. Vernon Street, Boston, the Society has branches at each of the following places: Amherst, Beverly, Brockton, Fall River, Greenfield, Haverhill, Ipswich, Lawrence, New Bedford, Northampton, Pittsfield and Worcester. Mr. John H. Sturgis, the treasurer, announced that the Society had closed its fiscal year with a deficit of $9,086.53. At the public meeting, Lieutenant Governor-elect Grafton D. Cushing, president of the Society, presided and Dr. Richard C. Cabot spoke on "The Root and Branch of Social Work."

CASES OF INFECTIOUS DISEASES reported to the Boston Board of Health for the week ending Dec. 1, 1914: diphtheria, 112, of which 8 were non-residents; scarlatina, 41; typhoid fever, 8, of which 1 was non-resident; measles, 109; tuberculosis, 38. The death rate of the reported deaths for the week was 15.84.

Case of Smallpox in Boston.—Another case of smallpox, in a 16 months baby, was discovered at Boston on Nov. 25 among Italian immigrants held in detention at quarantine from aboard the steamer *Cretic*, on which occurred the case reported last week.

A Vigorous Centenarian.—Richard Kimball Powers, of Lancaster, Mass., who is said to have been born on Nov. 26, 1810, at Sterling, Mass., celebrated recently his supposed 104th anniversary by chopping the wood necessary to cook his Thanksgiving dinner. He attributes his vigorous longevity to hard work, honesty and abstemiousness.

Bequest for Medical Science.—The will of the late Dr. Charles Sedgwick Minot, Stillman professor of comparative anatomy at the Harvard Medical School, was filed on Nov. 27 in the probate court at Dedham, Mass. It contained a bequest of $1000 for the improvement and increase of the embryological collection which he established at the Harvard Medical School, to which he has also left his scientific apparatus, books and pamphlets.

NEW YORK.

Public Instruction in Prevention of Tuberculosis.—In coöperation with the division of public health education of the Department of Health, the Board of Education recently arranged for a week of public instruction of the adults of the city in the prevention and care of tuberculosis, and this campaign of education was the most comprehensive of its kind ever undertaken. Some sixty illustrated lectures were given by physicians and nurses of the Health Department during the week beginning Nov. 29, in the public school buildings of the various borroughs; ten or a dozen lectures on each evening of the week except Sunday.

Mortality for Week Ending November 28, 1914.—During the week ending Nov. 28, 1914, there were 1389 deaths with a death rate of 12.98 as against 1288 deaths and a death rate of 12.51 during the corresponding week last year. This increase is due to the greater number of deaths from diphtheria and croup and diseases of the respiratory tract. The deaths from diarrheal diseases were slightly lower than those of last year, in spite of the fact that there were 26 more deaths of infants under one year than during the corresponding week last year.

The weekly rate is affected by so many factors that the slight weekly fluctuations in the number of deaths are of little importance. The important point is that the death rate for the first 48 weeks of 1914 is lower than that of the corresponding period in 1913.

Current Literature

Medical Record.

November 21, 1914.

1. Hecht, D. *The Public and the Profession: A Criticism.*
2. Holmes, B. *A Plea for a Research into the Possibility of the Cure of Dementia Precox by the Use of Serum Containing the Defensive Ferment.*
3. Lilienthal, H. *The Relation of Gynecology and Urology to General Surgery.*
4. *Fischer, L. *The Association of Follicular Tonsillitis with Acute Gastric Fever: A Clinical Study.*
5. Williams, E. H. *The Sexual Significance of Recent Fashions.*
6. Cunningham, W. P. *Face to Face.*
7. Amsden, H. H. *Vincent's Angina.*
8. Voorhees, I. W. *A Case of Acute Thyroiditis.*

4. Fischer asserts that the clinical association of benign follicular tonsillitis with gastric fever—loss of appetite, acetone breath, fever, meteorism, constipation—is very common. If a child presents these symptoms the tonsils should be carefully inspected and if hypertrophied treated as diseased tissue and a focus for future infection. He advises for these cases an alkaline laxative and locally one application of tincture of iodine to the throat. [L. D. C.]

New York Medical Journal.

November 21, 1914.

1. Gordon, A. *Insanity and Divorce.*
2. Pedersen, V. C. *Teratoma Testis with Tubercle Bacilli in the Urine.*
3. Waitzfelder, E. *Implantation of Pituitary Gland.*
4. Madigan, P. S. *The Solution of the Problem of Criminal Abortion.*
5. Berghausen, O. *Intraspinous Medication.*
6. Holland, A. L. *Hyperchlorhydria.*
7. Kauffer, H. J. *A New Method of Hastening Repair after Fracture.*
8. Jackson, J. A. *Need of More State Hospitals for the Insane.*
9. *Wainwright, J. M. *Rôle of the Cecum in Chronic Disorders in the Right Lower Abdomen.*
10. Gardner, J. A. *Tuberculosis of the Kidney.*
11. Cooke, C. H. *Early Pulmonary Tuberculosis.*
12. Lackner, R. J. *A New Poison-Containing Bottle.*
13. Loevenhart, A. S. *Certain Aspects of Vital Oxidation.*

9. Wainwright calls attention to the importance of the cecum in the causation of chronic disorders in the right lower abdomen. It is rarely justifiable, he says, to limit any operative interference to simple removal of a supposed chronic appendix unless the other organs in the right abdomen are carefully examined and found normal or unless the appendix itself shows unmistakable gross signs of disease. It will avail little to remove a normal appendix, if a dilated and movable cecum is left behind. [L. D. C.]

The Journal of the American Medical Association.

November 28, 1914.

1. Putnam, J. J. *Services to be Expected from the Psychanalytic Movement in the Prevention of Insanity.*

2. *GREGG, D. *Genetic Factors in One Hundred Cases of Psychoneurosis.*
3. SOUTHARD, E. E. *Notes on Public Institutional Work in Mental Prophylaxis, with Particular Reference to the Voluntary and "Temporary Care" Admissions and the "Not Insane" Discharges at the Psychopathic Hospital, Boston, 1912-1913.*
4. *LOWENBURG, H. *Efficiency of Sodium Chlorid in the Therapeutics of Bright's Disease. A Further Clinical Study.*
5. THOMAS, B. A. *The Rôle of Functional Kidney Tests and Preoperative and Postoperative Treatment in the Reduction of Prostatectomy Mortality.*
6. LESPINASSE, V. D. *The Relief of Sterility by Means of Permanent Epididymostomy, with the Formation of an Artificial Sac for the Storage of the Sperm.*
7. JACKSON, C. *The Direct Method of Intralaryngeal Operation.*
8. CURTIS, H. H. *Indirect Intralaryngeal Method for Removal of Benign Neoplasms.*
9. SKILLERN, R. H. *Method of Suspension (Killian).*
10. FORSYTHE, W. E. *Health Services in American Colleges and Universities.*
11. JOBLING, J. W., AND PETERSEN, W. *The Therapeutic Effect of Iodin.*
12. ORENSTEIN, A. J. *Contribution to the Study of the Value of Quininization in the Eradication of Malaria.*
13. MCGUIGAN, H. *A Colloidal Compound of Strychnin and Its Pharmacology.*
14. OGILVIE, H. S. *The Intraspinal Treatment of Syphilis of the Central Nervous System with Salvarsanized Serum of Standard Strength. Report of Cases.*
15. RICHARDSON, D. L. *The Prevention of Communicable Diseases in General Hospitals.*
16. LEVY, R. L. *Oil of Chenopodium in the Treatment of Hookworm Infections.*
17. BRAV, A. *Congenital Phthisis Bulbi, with Report of a Case.*
18. SWASEY, E. *A Severe Case of Exophthalmic Goiter, with Complete Recovery without Operation, Rest or Medication.*
19. COPELAND, G. G. *Traumatic Rupture of the Healthy Aorta without External Signs of the Cause of Death.*
20. CLARK, O. *Exophthalmic Goiter as a Clinical Manifestation of Hereditary Syphilis.*

2. Gregg finds that in psychoneurosis there practically always exists as an essential factor an acquired or hereditary tendency. Luetic, insane, neurotic, and alcoholic defects, in the order named, are the essential factors in the production of these tendencies.

4. Lowenburg finds that sodium chlorid neither produces nor increases water retention in either the nephritic or non-nephritic. It is curative in cases of edema from any cause provided the kidneys are not too severely damaged. It does not cause edema in marantic infants. When combined with an alkali and plenty of water it exerts a beneficent influence on all the symptoms of nephritis. It is dangerous to introduce a solution of an alkali under the skin as it is liable to produce sloughing. It is best administered by rectum or intravenously. [E. H. R.]

THE JOURNAL OF EXPERIMENTAL MEDICINE.

NOVEMBER 1, 1914.

1. *ROUS, P. *The Influence of Diet on Transplanted and Spontaneous Mouse Tumors.*
2. JOBLING, J. W., AND PETERSEN, W. *Bacterial Antiferments. Studies on Ferment Action.*
3. JOBLING, J. W., AND PETERSEN, W. *Lipoids as Inhibitors of Anaphylactic Shock. Studies on Ferment Action.*
4. PAPPENHEIMER, A. M. *Further Experiments upon the Effects of Extirpation of the Thymus in Rats, with Special Reference to the Alleged Production of Rachitic Lesions.*
5. MORGULIS, S., AND GIES, W. J. *The Calcium Content in Bones and Teeth from Normal and Thymectomized Albino Rats.*
6. FLEISHER, M. S., AND LOEB, L. *The Influence of Various Substances on the Growth of Mouse Carcinoma.*
7. FLEISHER, M. S., AND VERA, MIGUEL, AND LOEB, L. *Immunization against the Action of Substances Inhibiting Tumor Growth.*
8. LEIGHTON, W. E. *Do Substances Inhibiting Tumor Growth Exert a Retarding Influence on the Regeneration of the Skin?*

1. Rous found that large growths of certain strains of transplanted rat and mouse tumors were checked by underfeeding the host upon a special diet or in some cases by simple underfeeding. On the other hand, diet gave varied results in the case of spontaneous growths and the inhibition of growth in these tumors seemed rather attributable to a gradual malnutrition than to the diet. Consequently, at present at least, the work seems to have no direct clinical significance. [R. I. L.]

MÜNCHENER MEDIZINISCHE WOCHENSCHRIFT.

NO. 32. AUGUST 11, 1914.

1. *SCHMINCKE, A. *The Cause of Hemorrhoids.*
2. SATHOFF, V. L. *The Necessity of Uniform Temperature Measurements, and the Range Between Normal and Pathological Temperatures.*
3. WEGENER, E. *The Sex Specificity of Abderhalden's Reaction and the Effect of Narcotics on the Test.*
4. PORTER, A. E. *The Distribution of Ferments Which Split Fat and Lecithin in Various Organs.*
5. CHILAIDITI, D. *The Technic of Gynecological Roentgen Ray Treatment.* L
6. GREINCHER, H. *The Ionometer and Its Use in Measuring the Dosage of Roentgen Rays.*
7. GEIGEL, R. *An Improvement in Illuminating for Fluoroscopy.*
8. *GRIMM, K. *Taenia Saginata in Infancy.*
9. HEIDENHAIN, L. *Operation or X-ray Treatment?*

1. Schmincke describes the anatomy, histology and physiology of the area supplied by the hemorrhoidal plexus of veins. Normally, he believes, dilatation of the veins in this region must occur with defecation on account of the distribution of the blood vessels. Such physiological dilatation increases with age and becomes especially marked in individuals of constipated habit. The pathological condition known as hemorrhoids occurs when the feces press on the hemorrhoidal veins to such an extent as to interfere with proper emptying. At the same time the venous stasis is exaggerated by the increased abdominal pressure induced by the passage of a constipated stool.

The first abnormal anatomical change noted is hypertrophy of the walls of the veins to compensate for the increased venous pressure. Finally the veins become insufficient, edema and subsequent infection occur, and the clinical hemorrhoid is formed.

8. Grimm reports a case of taenia saginata in an infant ten and a half months old. The chief interest in the paper lies in Grimm's review of the literature dealing with similar cases. Taenia of different types have been noted in several infants, but the disease is by no means common. Two cases have been reported in which taenia were found in infants five days old. [R. F.]

NO. 33. AUGUST 18, 1914.

1. *MEYER, E. *Clinical and Experimental Studies on the Action Obtained by Salvarsan upon Congen-*

ital Syphilis of the Fetus through Treatment of the Mother.
2. DESSAUER, F. *Artificially Induced Gamma Rays.*
3. KÖCK, E. *Non-diphtheritic Laryngeal Stenosis in Children.*
4. TOBIAS, P. *The Relapsing Colic of Children.*
5. PASINI, A. *The Toxic Manifestations of Embarin.*
6. RIGLER. *The Quadratograph. An Apparatus to Assist X-ray Work.*
7 *STERNBERG, W. *An Esophagotherm for the Treatment of Stenosis.*
8. MÜLLER, C. *Operation or Ray Treatment?*

1. Meyer believes that the clinical examination of the mother affords no indication as to the existence of a fetal lues. Therefore in a suspected case, the syphilis must be treated during the entire pregnancy in order to obtain a viable child. Mercury alone has not afforded much protection against congenital syphilis. Better results have been obtained by the intensive treatment of the disease made possible by salvarsan. Since the outlook for obtaining a healthy child improves with the thoroughness of treatment, Meyer advises a course which includes at least 1.5 grams of salvarsan combined with .5 grams of salicylated mercury. Finally, the children of syphilitic mothers, even though they show no clinical or serological signs of the disease, must be treated for a considerable period after birth.

7. Sternberg has devised a bougie through which an electrical current passes, thus allowing the direct application of heat to an esophageal stricture. Sternberg considers this instrument of great advantage in the treatment of esophageal stenosis or spasm. Because of the hyperemia induced by the heat at the point of disease, a serous exudate is induced which quickly softens the infiltrated or scarred region and as a result a rapid dilatation is made possible.

[R. F.]

No. 34, AUGUST 25, 1914.

1. ROMBERG, E. *The Clinical Diagnosis of the Type of Pulmonary Tuberculosis.*
2. HESS, O. *Results with the Phenolsulphonephthalein Test for Renal Function.*
3. WEINER, S. *The Granular Form of the Virus of Tuberculosis.*
4. SCHANZ, F. *The Cause of Far-sightedness.*
5. *HAPPICH, C. *Insomnia.*
6. *WECHSELMANN, W. *A Critical Study of the Causes of Death Following Injections of Salvarsan.*

5. According to Happich's views disturbances of sleep are centered in the brain. Sleep depends on a passive hyperemia with diminished vascular tone, in contrast to the active hyperemia with increased vascular tone which occurs during mental effort. Sleeplessness, therefore, may depend on anatomical changes in the brain tissue which disturb the normal blood supply, or may be due to functional disturbances in the cerebral vaso-motor system.

To treat sleeplessness successfully, each individual case must be studied. The fundamental principle of treatment depends on re-educating the patient to sleep automatically, and thus the medicines used must vary according to the etiology of the symptom. For instance, in cerebral arteriosclerosis hypnotics are often without effect, while strophanthin or diuretin may induce sleep, and in toothache or rheumatic pain aspirin may be of value when other drugs are not.

It must be remembered that all hypnotics are variable in action and that immunity to any one is quickly obtained. Thus a series of different drugs in rapid succession should be tried, rather than an increasing dose of any one. Finally, one of the most satisfactory methods of using hypnotics is to give them in small and repeated doses during the day, rather than in a single large dose at night.

6. Wechselmann discusses "hypersensitiveness" to salvarsan as a cause of sudden death following the injection of the drug. He believes that it is more important to study the functions of living organs than to dispute about "idiosyncrasy" after death. In salvarsan treatment, the kidney is a most important organ. Acute infections, mercury, or alcohol may injure it to such an extent functionally that it cannot excrete arsenic and as a result, poisoning may occur. Hepatic or polyglandular insufficiency is rarer but may occur. Thus on the whole, Wechselmann advocates a careful functional study of salvarsan cases. If this is carried out, "hypersensitiveness" will be met with rarely.

[R. F.]

Obituary.

CHARLES SEDGWICK MINOT.

DEC. 23, 1852—Nov. 19, 1914.

IN America anatomy has long been taught as an adjunct of surgery. Only recently has it been recognized as an independent and growing science, requiring for its successful pursuit rare natural gifts not less than genius. In Europe, on the contrary, it has always held an honored place, and great anatomists have appeared in almost every country. In 1909, with a civic celebration, the city of Neuss dedicated a monument to "her greatest son," Theodor Schwann, famous for his researches in microscopic anatomy; and in 1900 Johannes Müller was similarly honored in Coblenz. Since that recent time, both His and Kölliker have ended their studies which have become an integral part of anatomical science. But in this particular field, America, until the present day, has produced no peer of these great men. The rarity in this nation of such achievement as that of Charles Sedgwick Minot brings home to us the profound importance of his work, which has now been completed. Even while oppressed by recent bereavement, we can trace with just pride the career of this eminent American anatomist.

Dr. Minot was born in Boston. His parental home is described as comprising "about thirty acres of land, sheltered by large trees and abundant shrubbery, including also some acres of swamp . . . It stood on the edge of the Great Forest, which then stretched to the Blue Hills and the Great Ponds in Canton and Braintree on the south." On this estate and in the surrounding country, he laid the foundation for his future scientific work by becoming "a good amateur naturalist." His first scientific publication was a brief description of the male of *Hesperia metea,* a small butterfly captured in Dorchester, of which species only the female had previously been recorded. This paper, presented to the Boston Society of Natural History on Feb. 24, 1869, was quickly followed by other studies of insects, including descriptions of new species. Later, in 1875, we find him at the Col-

lége de France studying the microscopic anatomy of the water-beetle, *Hyrdophilus piceus*, under the direction of Ranvier. Subsequently he described the histology of the locust and cricket (1880), together with the anatomy of the cotton-worm (1884), for the Entomological Commission at Washington. Finally, as a reminiscence of his early interest in insects, he published in 1901 certain notes on the larvae and pupae of Anopheles, made in 1879. At that time these mosquitoes were of no medical interest, but the curious habits of their larvae had attracted his attention, and he reared many of them to maturity.

After Minot had obtained the degree of Bachelor of Science from the Massachusetts Institute of Technology and had made his early studies of insects, he undertook physiological investigations with Dr. Henry P. Bowditch, then assistant professor at the Harvard Medical School. They published jointly in this Journal (May 21, 1874) a paper on the effects of anesthetics on the vaso-motor centres. Influenced no doubt by Professor Bowditch, for whom he had always the warmest friendship and the highest regard, he visited the physiological institute at Leipzig; and under the direction of Carl Ludwig, who had been Bowditch's teacher, he studied the production of carbonic acid in resting and active muscle. Thirty years later he referred to Professor Ludwig as the greatest teacher of the art of scientific research whom he had ever known. After returning to America he conducted an extensive series of experiments on tetanus, published in 1878, and in that year he received from Harvard University the degree of Doctor of Science, for his work on the physiology of muscular contraction. This marked the end of his strictly physiological studies. Although well trained in chemistry and initiated in physiology by Bowditch and Ludwig, morphology appeared to him as even more attractive.

While in Leipzig, Minot studied also in the zoölogical laboratory under Leuckhart, completing an investigation of the turbellarian worms begun at Würzburg under Semper. He had mastered the latest methods of microscope technic and had caught the spirit of the German universities. In his paper on the study of zoölogy in Germany (1877), he wrote:—

"The universities, unlike many of our colleges, are not mere high-schools, but are the centres of intellectual activity. The distinguishing feature of them is their organization, which gives to original research the highest rewards, and makes everything else subordinate to investigation . . . The rigid adherence to this system has made the German universities the home of the highest science."

Realizing how little the American schools had contributed toward equipping him for his life work, which he was now ready to undertake, he later said:—

"In regard to our schools there prevails the miserable delusion that they are good . . . Can we not plan a system of school education in which science shall have its place, and by which our children shall acquire some information about themselves, the world around them, and at the same time be disciplined in observation and reasoning?"

It was to the great task of raising the standards of higher education in America, particularly in his own field, that Dr. Minot had committed himself when, in 1880, he was appointed Lecturer in Embryology at the Harvard Medical School. He took charge of the department of histology, which was then equipped with 18 Hartnack microscopes and supported by an annual appropriation of fifty dollars. From this beginning, with incessant labor on his part and later on the part of his assistants, he has seen his hopes realized, until the opportunities for study and investigation now provided in his laboratories are scarcely equalled. Especially notable is his wonderful collection of over nineteen hundred embryos of various animals, cut into many thousands of sections, each of which is numbered and catalogued. He has described this collection as "a sort of cyclopedia of vertebrate embryology to which one can turn at any time and get the desired information as to the principal features of development of any structure whatsoever." Already it has been used by Professor Minot and many others for important investigations.

At the same time the instruction of beginners in embryology has been facilitated by preparing one hundred and fifty complete series of sections of pig embryos of a stage most interesting to students of human anatomy. The use of mammalian embryos, rather than those of chicks, was an innovation, and called for the preparation of a special *Laboratory Text-Book of Embryology*. This was issued in 1903, many years after Minot had begun to use pig embryos, and being the first text-book of its kind, it has led to a more general laboratory study of mammalian embryology both in colleges and medical schools. Knowing that the book was in preparation, Professor Minot's assistants and pupils supplied him freely with reconstructions, often made on their own initiative. These were very acceptable, since he himself never cared to pursue this rather mechanical method of investigation. He spent the spring of 1914 in preparing a third edition of the text-book, which was left nearly ready for the printer.

A far more important book, which placed Minot at once in the front rank of embryologists, was his well-known *Human Embryology*, published in 1892,—the "result of ten years' labor." This was an ambitious attempt to present in one large volume a summary of all that was then known concerning human development, with exact bibliographical references to every paper cited (nearly a thousand). It in-

cluded also numerous contributions based upon the author's personal observations, especially in the chapters on the placenta and embryonic membranes. When this work was issued in its German edition in 1894, Professor His described it as substantial throughout, with the facts everywhere in the foreground. "Minot's work," he wrote, "is at present the fullest embryology of man which we possess, and it will retain its value as a bibliographical treasure-house even after its contents in many parts have been superseded." By exposing the numerous gaps in embryological knowledge, and by challenging many current opinions it served as a great impetus to further research. A revision was never undertaken.

Of Professor Minot's briefer papers none perhaps is more characteristic than his treatment of "sinusoids." Like other embryologists he had been familiar with the lacunar vessels in the embryonic liver, Wolffian body and elsewhere, and they had in fact been figured in his *Human Embryology* (1892). It remained for him to bring them together as a class in 1900, under a new name, and to describe them in a paper bearing the rather startling title,— "On a hitherto unrecognized form of blood circulation without capillaries in the organs of Vertebrata." For the first time the striking and important differences between slender capillaries imbedded in connective tissue layers and wide lacunar blood spaces closely applied to the parenchyma of an organ, were adequately presented, and they are now well known. This publication, like many others by Dr. Minot, did not require special stains or the use of rare material. It illustrates what Lowell has described as "the divine faculty to see what everybody can look at," and the observations have both anatomical and physiological significance.

A series of studies in which Professor Minot took the greatest interest were concerned with the nature of growth. They began in 1879 with a paper on "growth as a function of cells," in which it is stated that during growth "two fundamentally different processes display themselves: the gradual *senescence* which continually hinders and delays the multiplication of cells and their vital acts, at last supressing them altogether at the moment of death; before senescence conquers, the sexual products are thrown off and effect the process of *rejuvenation.*"

Senescence and rejuvenation were studied by tabulating the weights of guinea-pigs from birth to old age, and of rabbit embryos up to the time of birth, using weight as a measure of growth. The conclusion was drawn that the fertilized ovum is endowed with an enormous power for growth, over ninety-eight per cent. of which has been lost at the time of birth. The remaining two per cent. is largely exhausted in infancy. Therefore he concludes that "senescence is at its maximum in the very young stages and the rate of senescence diminishes with age." He protests against "the medical conception that age is a kind of disease," chronic and incurable, of any such nature as intestinal intoxication or arterio-sclerosis. On the contrary he finds that it has a cytological cause, equally operative in the lower animals which have neither intestines or arteries and in man; and he ascribes senescence to the increase and differentiation of cytoplasm as compared with nucleoplasm.

In 1901 he proposed "the new term *cytomorphosis* to designate comprehensively all the structural alterations which cells, or successive generations of cells may undergo from the earliest undifferentiated stage to their final destruction." His latest works on this subject, aptly characterized as "thoughtful and suggestive," refer to cytomorphosis as a most promising field for further study, and at the time of his death, plans had been made for careful investigations to test the validity of his cytomorphic hypothesis concerning age.

Altogether Professor Minot published no less than one hundred and eighty scientific notes and papers, including a considerable number of presidential and other addresses. The latter have been collected and issued in German translation under the title "*Die Methode der Wissenschaft und andere Reden*" (Jena, 1913). Their wide scope is indicated by such subjects as "Ideals of Medical Education," "The Embryological Basis of Pathology" and "The Problem of Consciousness in its Biological Aspects." His addresses and lectures were delivered with characteristic ease and dignity, commanding at once respectful attention.

Appreciating the value of scientific societies in promoting research, he was deeply interested in the organization and development of those in America, and at different times was chosen president of the Naturalists, the Anatomists and the American Association for the Advancement of Science. He was a member of many others, including the National and American Academies and learned societies in Belgium, England, France, Germany and Italy. Honorary degrees were conferred upon him by Yale in 1899, Oxford (1902), the University of Toronto (1904) and St. Andrew's University in Scotland (1911).

Every anatomist in America will find his work facilitated by what Minot has done in inventing microtomes, developing the means of publication, and encouraging research through societies and funds, of which the small Thompson Fund entrusted to him may serve as a model for the administration of much greater foundations. It was altogether fitting that, as exchange professor to Berlin, he should appear as the official representative of anatomy in America, to present the results of American investigations made during the past decade. Our interests were in the hands of a friend and skilful advocate, who showed that a good beginning had been made,

and expressed reasonable hopes for a great future.

After returning from Europe, failing health prevented the energetic activities of earlier years, but we find the same interests as in boyhood. As president of the Boston Society of Natural History, where his first paper had been presented, he continued to direct the transformation of the old collections into those which are creditable to the city, showing how much may be accomplished with inadequate endowment, if wisely managed. He took great delight in this society and in all that it stands for. He was interested also in horticulture, and in his gardens in Milton he cultivated rare varieties of peonies with unusual success. All these were kindred interests—the natural diversions of a genuine biologist. Retaining the broad outlook of the earlier naturalists, he devoted himself intensively to a narrow field of scientific inquiry, and has made an impressive contribution to his chosen science of anatomy. "Great professors make a great school" as Professor Minot once said, and he has given to the Harvard Medical School an international renown.

FREDERICK T. LEWIS.

Correspondence.

FOOT AND MOUTH DISEASE AND MILK.

BOSTON, Nov. 27, 1914.

Mr. Editor: In your editorial on Foot and Mouth Disease in your issue of Nov. 26th, we notice on page 828 the statement: "The Boston Board of Health adopted an order recommending the sterilization by boiling of all uncertified milk supplies before they are used as food for human beings." This is a very inaccurate paraphrase of the orders passed by the Board of Health and carries a meaning very different from that of the order passed. The order passed by the Board of Health is as follows:

"BOARD OF HEALTH.

"Boston, November 16, 1914.

"At a meeting of the Board of Health held this day it was voted that

"On account of the prevalence of the foot and mouth disease, and for the safety of milk users, the Board of Health recommends that for the present all supplies of raw milk be boiled before used as food.

"A true copy. Attest: H. F. SLACK, *Secretary.*"

Yours truly,

C. F. WHITING.

Miscellany.

HERTER LECTURES.

Under the auspices of the Herter Foundation of the University and Bellevue Hospital Medical College a series of lectures will be given on December 10, 11, 14 and 15, at 4 o'clock, at the Carnegie Laboratory, 338 East 26th Street, by Professor Lafayette B. Mendel, Ph.D., of Yale University, on the subject "Aspects of the Physiology and Pathology of Growth."

HARVEY SOCIETY.—The fifth lecture in the current series before the Harvey Society will be given at the New York Academy of Medicine, on Saturday evening, Dec. 12, by Prof. L. J. Henderson, of Harvard University, on "The Excretion of Acid in Health and Disease."

RECENT DEATHS.

DR. CLINTON WAGNER, a retired New York physician of prominence, died in Geneva, Switzerland, on November 27. He was born in Baltimore, Md., in 1840. During the Civil War he served as surgeon-in-chief of the fifth corps, Army of the Potomac, and after the war spent two years in the study of laryngology in London, Paris and Vienna. Dr. Wagner was the founder of the New York Laryngological Society, stated to be the first of its class in the world, and he established the Metropolitan Throat Hospital. He was also largely instrumental in the organization of the American Laryngological Society, and in 1882 he became the first professor of laryngology and rhinology in the New York Post-Graduate Medical School. He contributed much to the literature of his specialty, in which he was recognized as an authority in Europe, as well as in America. He is survived by his widow.

DR. CHARLES WOOD MCMURTRY, of New York, died on November 24, after an operation for appendicitis. He was a native of Pittsburg, and was graduated from the Harvard Medical School in 1897. He was a promising specialist in diseases of the skin, and at the time of his death held positions at the Vanderbilt Clinic and the dermatological clinic of St. Luke's Hospital.

DR. ROBERT MCNEILLY, a well-known New York practitioner, died on November 26, at the age of 83. He was born in the North of Ireland and was graduated from the medical department of the University of Pennsylvania in 1863. During the Civil War he served as assistant surgeon of an Ohio regiment.

DR. FRED VAN MAGNESS, of Chelsea, Mass., a graduate of the Harvard Medical School in 1904, died of pneumonia at his home in Everett, Mass., on Nov. 30, 1914, aged 34 years. He was supreme medical examiner for the Knights of Pythias. He was born in Boston on Sept. 24, 1880.

DR. WARREN MORRIS BABBITT, who died of pneumonia on November 26 in South Braintree, Mass., was born at Taunton, Mass., in 1832. During the Civil War he served as assistant surgeon of the Fifty-fifth Massachusetts Regiment, and later as surgeon of a New York regiment. He is survived by two daughters.

DR. JAMES TRUMAN, who died on November 26 at Philadelphia, was born in 1826. He was a former dean of the dental department of the University of Pennsylvania, and had edited a number of dental publications.

BOOKS AND PAMPHLETS RECEIVED.

A Text-book of Diseases of the Nose and Throat, by D. Braden Kyle, A.M., M.D. W. B. Saunders Company. 1914.

The Heart in Early Life, by G. A. Sutherland, M.D. Oxford University Press. 1914.

Precis de Chirurgie de Guerre par Edmond Delorme. Masson et Cie, Editeurs. 1914.

Mellon Institute of Industrial Research and School of Specific Industries. Smoke Investigation. Bulletin No. 9. Papers on the Influence of Smoke on Health. Edited by Oskar Klotz and Wm. Charles White. University of Pittsburg, Pittsburg, Pa. 1914.